(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 February 2006 (09.02.2006)

PCT

(10) International Publication Number
WO 2006/015258 A2

(51) International Patent Classification:
C12N 9/00 (2006.01)

(21) International Application Number:
PCT/US2005/027084

(22) International Filing Date: 28 July 2005 (28.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/592,297	28 July 2004 (28.07.2004)	US
60/592,269	29 July 2004 (29.07.2004)	US

(71) Applicant *(for all designated States except US)*: **COLD SPRING HARBOR LABORATORY** [US/US]; One Bungtown Road, Cold Spring Harbor, NY 11724 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **JOSHUA-TOR,Leemor** [IL/US]; 28 Chestnut Street, Huntington, NY 11743 (US). **SONG, Ji-Joon** [KR/US]; 1 Bungtown Road, Cold Spring Harbor, NY 11724 (US). **HANNON, Gregory, J.** [US/US]; 34 Griffith Lane, Huntington, NY 11743 (US). **LIU, Jidong** [CN/US]; Cold Spring Harbor, NY (US). **CARMELL, Michelle, A.** [US/US]; Nesconset, New York (US). **RIVAS, Fabiola** [BO/US]; Huntington, NY (US). **MARSDEN, Carolyn** [US/US]; Northport, New York (US).

(74) Agents: **HOLMES, Jennifer** et al.; Fish & Neave IP Group of, Ropes & Gray LLP, One International Place, Boston, MA 02110-2624 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

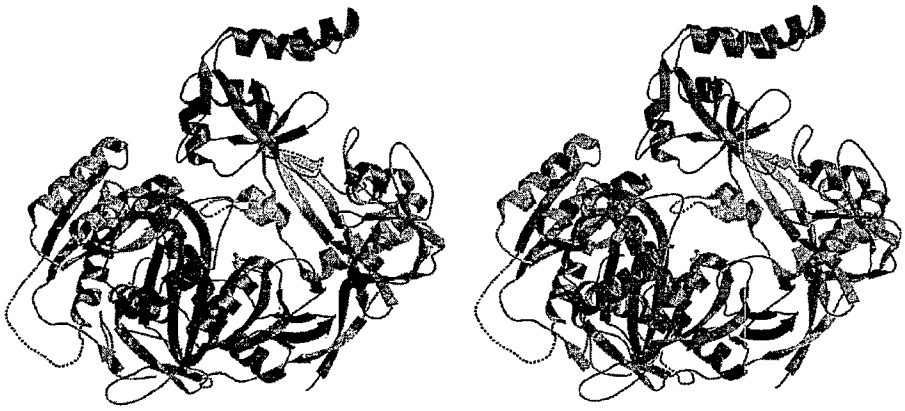
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND COMPOSITIONS RELATED TO ARGONAUTE PROTEINS



(57) Abstract: This invention provides methods and compositions related to Argonaute proteins and, in certain embodiments, the applications of these methods and compositions to treatment and therapeutics based on RNAi.

WO 2006/015258 A2

METHODS AND COMPOSITIONS RELATED TO ARGONAUTE PROTEINS

RELATED APPLICATIONS

This application claims the benefit of priority to U.S. Provisional Patent Application Nos. 60/592,269, filed on July 29, 2004, and 60/592,297, filed on July 28, 2004, which applications are hereby incorporated by reference in their entireties.

BACKGROUND OF THE APPLICATION

The presence of double-stranded RNA (dsRNA) in most eukaryotic cells provokes a sequence-specific silencing response known as RNA interference (RNAi) (G.J. Hannon, Nature 418, 244 (2002); A. Fire et al., Nature 391, 806 (1998)). The dsRNA trigger of this process can be derived from exogenous sources or transcribed from endogenous non-coding RNA genes that produce microRNAs (miRNAs) (Hannon, *supra*; G. Hutvagner et al., Curr. Opin. Genet. Dev. 12, 225 (2002)). RNAi begins with the conversion of dsRNA silencing triggers into small RNAs of ~21-26 nt in length (A. Hamilton et al., Embo J. 21, 4671 (2002)). This is accomplished by processing of triggers by specialized RNaseIII family nucleases, Dicer and Drosha (E. Bernstein et al., Nature 409, 363 (2001); Y. Lee et al., Nature 425, 415 (2003)). Resulting small RNAs join an effector complex, known as RISC (RNA-Induced Silencing Complex) (S.M. Hammond et al., Nature 404, 293 (2000)). Silencing by RISC can occur via several mechanisms. In flies, plants and fungi, dsRNAs can trigger chromatin remodeling and transcriptional gene silencing (M.F. Mette et al., Embo J. 19, 5194 (2000); I.M. Hall et al., Science 297, 2232 (2002); T. Volpe et al., Science 22, 22 (2002); M. Pal-Bhadra et al., Mol. Cell 9, 315 (2002)). RISC can also interfere with protein synthesis, and this is the predominant mechanism used by miRNAs in mammals (P.H. Olsen et al., Dev. Biol. 216, 671 (1999); D.P. Bartel, Cell 116, 281 (2004)). However, the best-studied mode of RISC action is mRNA cleavage (T. Tuschl et al., Genes Dev. 13, 3191 (1999); P.D. Zamore, Cell 101, 25 (2000)). When programmed with a small RNA that is fully

complementary to the substrate RNA, RISC cleaves that RNA at a discrete position, an activity that has been attributed to an unknown RISC component, "Slicer" (S.M. Elbashir et al., Embo J. 20, 6877 (2001); J. Martinez et al., Cell 110, 563 (2002)). Whether or not RISC cleaves a substrate can be determined by the degree of complementarity between the siRNA and mRNA, as mismatched duplexes are often not processed (Elbashir et al., *supra*). However, even for mammalian miRNAs, which normally repress at the level of protein synthesis, cleavage activity can be detected with a substrate that perfectly matches the miRNA sequence (G. Hutvagner et al., Science 1, 1 (2002)). This prompted the hypothesis that all RISCs are equal with the outcome of the RISC-substrate interaction being determined largely by the character of the interaction between the small RNA and its substrate.

RISC contains two signature components. The first is the small RNA, which co-fractionated with RISC activity in Drosophila S2 cell extracts (Hammond et al., *supra*) and whose presence correlated with dsRNA-programmed mRNA cleavage in Drosophila embryo lysates (Tuschl et al., *supra*; Zamore et al., *supra*). The second is an Argonaute protein, which was identified as a component of purified RISC in Drosophila (S.M. Hammond et al., Science 293, 1146 (2001)). Subsequent studies have suggested that Argonautes are also key components of RISC in mammals, fungi, worms, protozoans and plants (Martinez et al., *supra*; M.A. Carmell et al., Nat. Struct. Mol. Biol. 11, 214 (2004)). To date, the identity of "Slicer" and the function of Argonaute proteins are unknown.

BRIEF SUMMARY OF THE APPLICATION

This application provides methods and compositions related to Argonaute proteins.

A first aspect of application provides a crystalline Argonaute. Certain embodiments provide an isolated and purified Argonaute protein having a three-dimensional structure defined by the atomic coordinates such as for example as shown in Table 3. The crystalline Argonaute may comprise an archae Argonaute protein. Alternatively, the crystalline Argonaute may comprise a mammalian Argonaute protein, e.g., a human Argonaute protein such as human Ago-2.

Examples of mammalian Argonaute proteins may be Ago-1, Ago-2, Ago-3, or Ago-4.

In certain embodiments, a crystalline Argonaute may comprise an Argonaute protein having an amino acid sequence that is 95% identical to SEQ ID NO: 2 (or human Ago-2) or a homologue, fragment, variant, or derivative thereof. Alternatively, a crystalline Argonaute may comprise an Argonaute protein having an amino acid sequence that is 95% identical to SEQ ID NO: 2 (or human Ago-2) or a homologue, fragment, variant, or derivative thereof.

Certain embodiments provide a crystalline Argonaute comprising a three-dimensional structure defined by all or a portion of the atomic co-ordinates such as for example as set forth in Table 3.

The application also provides native crystals, derivative crystals or co-crystals, that have a root mean square deviation ("r.m.s.d.") of less than or equal to about 1.5 Angstrom when superimposed, using backbone atoms (N, Cα, C and O), on the structure coordinates listed in Table 3.

A crystalline Argonaute of the application may comprise at least two domains, e.g., a PAZ domain and a PIWI domain. A PIWI domain comprises a carboxylate triad formed by the motif "DDX" (X refers to a third amino acid, e.g., E). A crystalline Argonaute of the application may comprise a PIWI domain having a carboxylate triad formed by D597, D669, and a third amino acid.

A crystalline Argonaute of the application may comprise the following overall architecture: the N-terminus, middle, and PIWI domains form a crescent-shaped base; and the PAZ domain is positioned above the crescent shaped base; resulting in a cleft between said crescent-shaped base and the PAZ domain.

In certain embodiments, a crystalline Argonaute permits an X-ray crystallography resolution better than 2.25 Angstrom.

In certain embodiments, a crystalline Argonaute is soaked with one or more agents to form co-complex structures.

A crystalline Argonaute may comprise a PIWI domain having an active site defined by two or more amino acids, such as for example the "DDX" (X representing a third amino acid, e.g., E) triad. A crystalline Argonaute may comprise a PAZ domain having an active site defined by two or more amino acids. In certain embodiments, an active site is capable of accommodating an agent, e.g., a ligand or an inhibitor. A ligand or an inhibitor may be a nucleic acid molecule, a peptidomimetic, or a small organic molecule. A ligand or an inhibitor may be soaked in to form a co-complex. A nucleic acid molecule that is a ligand or an inhibitor can be a single stranded RNA molecule, e.g., a single stranded RNA molecule comprising between 15-50 nucleotides.

The application further provides an isolated complex comprising an Argonaute protein and a single stranded RNA molecule hybridized to its target nucleic acid. In certain embodiments, the single stranded RNA molecule is bound to the PAZ domain of the Argonaute protein. In certain embodiments, the target nucleic acid further interacts with the crescent-shaped base of the Argonaute protein.

A further aspect of the application provides a method of determining the three-dimensional structure of an Argonaute protein or a mutant, derivative, variant, analogue, homologue, sub-domain or fragment thereof. The method may comprise aligning the amino acid sequence of the Argonaute mutant, derivative, variant, analogue, homologue, sub-domain or fragment with the amino acid sequence of PfAgo or as set forth in SEQ ID NO: 5 to match homologous regions of the amino acid sequences. The method may further comprise modeling the structure of the matched homologous regions of said target Argonaute protein of unknown structure on the corresponding regions of the Argonaute protein structure as defined by the atomic co-ordinates as set forth in Table 3. The method may also comprise determining a conformation for the Argonaute mutant, derivative, variant, analogue, homologue, sub-domain or fragment which substantially preserves the structure of said matched homologous regions.

A further aspect of the application provides a method of identifying an agent that binds an Argonaute protein. The method may comprise applying a 3-dimensional molecular modeling algorithm to the atomic coordinates of an

Argonaute protein shown in Table 3 to determine the spatial coordinates of the binding pocket of the Argonaute protein. The method may further comprise electronically screening the stored spatial coordinates of a set of candidate agents against the spatial coordinates of the Argonaute protein binding pocket to identify agents that can bind to the Argonaute protein.

The application also provides a computer-based method for the analysis of the interaction of a molecular structure with an Argonaute protein. The method may comprise providing a structure comprising a three-dimensional representation of said Argonaute protein or a portion thereof, which representation comprises all or a portion of the coordinates set forth in Table 3. The method may further comprise providing a molecular structure to be fitted to said Argonaute protein structure. The method may also comprise fitting the molecular structure to the Argonaute protein structure, e.g., as set forth in the three-dimensional representation.

The application also provides a computer-readable storage medium encoded with the atomic coordinates or an Argonaute protein as shown in Table 3. Other embodiments also provide a data array comprising the atomic coordinates of an Argonaute protein as set forth in Table 3.

The application further provides an electronic representation of a crystal structure of an Argonaute protein. In certain embodiments, the electronic representation may contain atomic coordinate set forth in Table 3. Certain embodiments also provide an electronic representation of a binding site of the Argonaute protein. The binding site may locate in or be defined by the PAZ and/or PIWI domain or a portion thereof. Certain embodiments also provide an electronic representation of a domain of the Argonaute protein, e.g., a PIWI domain and/or a PAZ domain. Certain embodiments also provide an electronic representation of an agent in a binding site of an Argonaute protein, e.g., an active site of the Argonaute protein.

The crystal structure, the electronic representation, as well as other aspects of the application also relate to a method for identifying, designing, and/or optimizing

an RNAi construct or RNAi therapeutic of the invention, e.g., to improve an RNAi therapeutic's pharmacokinetic and/or pharmacodynamic profile.

Another aspect of the application relates to a method of obtaining a crystal formed by an Argonaute protein. The crystal may be grown using a precipitant. The crystal may be grown in a buffer, the pH of which buffer may be varied. The crystal may also be grown in the presence of a ligand or an inhibitor that interacts with the Argonaute protein, e.g., a domain of the Argonaute protein. The quality of the crystal can be improved by microseeding.

A further aspect of the application relates to a method of identifying an agent that modulates the activity of an RNAi construct. The method may comprise identifying an agent that modulates the expression and/or activity of an Argonaute protein. The method may involve an Argonaute protein expressed in a cell. The expressed Argonaute protein may be endogenous or exogenous to the cell. In certain embodiments, the agent can modulate (e.g., increase) the RNase activity of the Argonaute protein. The agent may alternatively or further modulate (e.g., increase) the expression of said Argonaute gene. In certain embodiments, an agent modulates the RNase activity and/or expression of an Argonaute protein in a tissue or cell type-specific manner.

In certain embodiments, the application relates to a method of identifying an agent that modulates the activity of an RNAi therapeutic. The method may comprise identifying an agent that modulates the expression and/or activity of an Argonaute protein. The method may involve an Argonaute protein expressed in a cell. The expressed Argonaute protein may be endogenous or exogenous to the cell. In certain embodiments, the agent can modulate (e.g., increase) the RNase activity of the Argonaute protein. The agent may alternatively or further modulate (e.g., increase) the expression of said Argonaute gene. In certain embodiments, an agent modulates the RNase activity and/or expression of an Argonaute protein in a tissue or cell type-specific manner.

In certain embodiments, an RNAi construct or an RNAi therapeutic attenuates the expression of a target nucleic acid molecule. The attenuation may be

by 2, 3, 5, 10, or higher fold. The target nucleic acid molecule may comprise an endogenous nucleic acid molecule. Alternatively, the target nucleic acid molecule is a heterologous to the genome of the cell. The heterologous nucleic acid molecule may be a nucleic acid from a pathogen.

An RNAi construct or an RNAi therapeutic of the application may comprise a nucleotide sequence at least 15 nucleotides in length that hybridizes to a target nucleic acid molecule. In certain embodiments, an RNAi construct or an RNAi therapeutic may comprise a hairpin nucleic acid. An RNAi construct or an RNAi therapeutic of the application may also comprise a promoter operably linked to a nucleotuide sequence that hybridizes to a target nucleic acid molecule. The promoter may be tissue or cell type-specific.

A further aspect of the application relates to a method of identifying an agent that potentiates the activity of an RNAi construct. The method may comprise identifying an agent that increases the expression and/or activity of an Argonaute protein. The agent may increase the expression and/or activity of an Argonaute protein in a tissue or cell type-specific manner.

Certain embodiments provides a method of identifying an agent that potentiates the activity of an RNAi therapeutic. The method may comprise identifying an agent that increases the expression and/or activity of an Argonaute protein. The agent may increase the expression and/or activity of an Argonaute protein in a tissue or cell type-specific manner.

Another aspect of the application provides a method of identifying an agent that modulates the activity of an RNAi construct. The method may comprise providing an isolated or recombinant Argonaute protein and assaying the RNase activity of the Argonaute protein in the presence of a candidate agent. A change in the RNase activity of the Argonaute protein in the presence of a candidate agent is indicative of the candidate agent capable of modulating the activity of the RNAi construct. The change may be relative to the RNase activity of the Argonaute protein in the absence of the candidate agent or a baseline or control level of the RNase activity of Argonaute protein. The method may involve an Argonaute

protein expressed in a cell. Alternatively, the method may involve an isolated or purified Argonaute protein. The method may further comprise determining the RNase activity of said Argonaute protein in the absence of a candidate agent. The identified agent may modulate the activity of an RNAi construct in a tissue or cell type-specific manner.

Certain embodiments provide a method of identifying an agent that modulates the activity of an RNAi therapeutic. The method may comprise providing an isolated or recombinant Argonaute protein and assaying the RNase activity of the Argonaute protein in the presence of a candidate agent. A change in the RNase activity of the Argonaute protein in the presence of a candidate agent is indicative of the candidate agent capable of modulating the activity of the RNAi therapeutic. The change may be relative to the RNase activity of the Argonaute protein in the absence of the candidate agent or a baseline or control level of the RNase activity of Argonaute protein. The method may involve an Argonaute protein expressed in a cell. Alternatively, the method may involve an isolated or purified Argonaute protein. The method may further comprise determining the RNase activity of said Argonaute protein in the absence of a candidate agent. The identified agent may modulate the activity of an RNAi construct in a tissue or cell type-specific manner.

A further aspect of the application provides a composition for targeted gene inhibition comprising an agent that modulates the RNase activity of an Argonaute protein. The composition may further comprise an RNAi construct or an RNAi therapeutic targeting a gene. In certain embodiments, an agent may potentiate the RNase activity of the Argonaute protein. Alternatively, an agent may inhibit the RNase activity of the Argonaute protein. In certain embodiments, the RNAi construct or therapeutic may target a gene in a first tissue or cell type; the identified agent may potentiate the RNase activity of the Argonaute protein in said first tissue or cell type. In certain embodiments, the identified agent may inhibit the RNase activity of the Argonaute protein in a second tissue or cell type.

The application also provides a pharmaceutical preparation comprising the compositions described herein and a physiologically acceptable carrier.

A further aspect of the invention relates to a cell line that overexpresses an Argonaute protein. The cell line of claim may overexpress a mammalian Argonaute protein, e.g., a human Agonaute protein. A mammalian Agonaute protein may be Ago-1, Ago-2, Ago-3, or Ago-4. The cell line may alternatively overexpress an Argonaute protein having an amino acid sequence that is 95% identical to an amino acid sequence as set forth in SEQ ID NOs.: 1-4, or a homologue, fragment, variant, or derivative thereof. The cell line may alternatively overexpress an Argonaute protein encoded by a nucleic acid molecule having a sequence that is 95% identical to a nucleic acid sequence as set forth in any one of SEQ ID NOs.: 1-4. The cell line may alternatively overexpress an Argonaute protein encoded by a nucleic acid molecule that hybridizes under high stringency conditions to a nucleic acid sequence as set forth in any one of SEQ ID NOs.: 1-4. The cell line may alternatively overexpress an Argonaute protein having an amino acid sequence set forth in any one of SEQ ID NOs.: 1-4.

Another aspect of the application relates to a cell line that expresses a mutant Argonaute protein comprising an amino acid sequence that is different from a naturally-occurring Argonaute protein.

A further aspect of the application relates to a host (e.g., a cell or an animal) wherein the expression of an endogenous Argonaute protein is controlled by, e.g., a transgene (or a nucleic acid construct such as for example the construct based on the Puro PGK vector described herein).

The application also provides an assay for identifying nucleic acid sequences for conferring a particular phenotype in a cell, comprising constructing a library of nucleic acid sequences oriented to produce double stranded RNA. The assay may further comprise ntroducing a dsRNA library into a culture of target cells. The assay may also comprise identifying members of the library which confer a particular phenotype on the cell, and identifying the sequence from the cell which is identical or homologous to the library member.

Another aspect of the invention provides a nucleic acid composition comprising a first nucleic acid comprising an RNAi construct and a second nucleic

acid encoding an Argonaute protein. The RNAi construct may comprise a nucleotide sequence encoding a single-strand siRNA; the nucleotide sequence may be operably linked to a promoter. In certain embodiments, the second nucleic acid encodes a human Argonaute protein and may be operably linked to a promoter. Alternatively, the second nucleic acid may encode a non-naturally-occurring Argonaute protein. In certain embodiments, the RNAi construct may be tissue or cell type-specific. The promoters may be tissue or cell type-specific.

A further aspect of the application provides a cell expressing any of the nucleic acid compositions described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows the crystal structure of *Pyrococcus furiosus* Argonaute. Stereo ribbon representation of Argonaute with the N-terminal domain shown in blue, the "stalk" in light blue, the PAZ domain in red, the middle domain in green, the PIWI domain in purple and the interdomain connector in yellow. The active site residues are drawn in stick representation. Disordered loops are drawn as dotted lines. The N-terminal, middle and PIWI domains form a crescent base. The "stalk" holds the PAZ domain above the crescent base and the interdomain connector cradles the molecule. This figure as well as figures 2A, 3A,B, 5B were prepared with BobScript (60), MolScript (61) and Raster3D (62, 63).

Figs. 2A-2B show that the PAZ domains of PfAgo and hAgo1 have very similar structures. (Fig. 2A) Stereo diagram of the superposition of Ca atoms from the PAZ domain of PfAgo in shown in red and the PAZ domain of hAgo1 shown in gray. Dotted lines represent disordered regions. (Fig. 2B) Sequence alignment of the PAZ domains of PfAgo, hAgo1 and DmAgo2 based on the structural superposition of the three domains. The sequence of PfAgo-PAZ domain could not be readily aligned with PAZ domains from other species without knowledge of the structure. The secondary structure elements for PfAgo are shown above the sequence.

Figs. 3A-3C show that PIWI is an RNase H domain. (Fig. 3A) Ribbon diagrams of the PIWI domain, *E. coli* RNase HI and *M. jannaschii* RNase HII. The three

structures were superimposed and shown in a similar view with the secondary structure elements of the canonical RNase H fold in color. The active site residues are shown in stick representation. (Fig. 3B) A close-up view of the active sites. This view is rotated ~180° compared to the view in A. One active site aspartate is always located on β1 of the fold (the red strand) in this family of proteins and another aspartate is always located on β4 of the fold (the green strand). The third active site carboxylate, a glutamic acid, varies in its position. The Mg^{2+} ion in RNase HI is shown as a pink sphere. A strong difference electron density found in the active site of PIWI that was assigned as a water molecule is shown as a green sphere. (Fig. 3C) Sequence alignment of the PIWI domains from Pf Argonaute and the four human Argonaute proteins. Invariant residues are highlighted in purple and conserved residues are highlighted in blue. The secondary structure elements are shown above the structure. The conserved active site carboxylate residues are marked by a red asterisk.

Figs. 4A-4B show siRNA binding. (Fig. 4A) A 5'-phosphorylated ss-siRNA (4 nM) was radiolabled by phosphorylation with γ-^{32}P-ATP and hybridized with an unlabeled complementary strand to yield a ds-siRNA and was gel purified. The ss- and ds-siRNAs were UV-crosslinked to PfAgo and the adducts were resolved by SDS-PAGE. PfAgo binds preferentially to the ss-siRNA compared to the ds-siRNA. (Fig. 4B) Competition experiments were performed with the same labeled ss-siRNA and UV-crosslinking to PfAgo in the presence of increasing amounts of the indicated competitors (from 0 to 400 nM), showing preferential binding to a 5'-phosphorylated ss-siRNA compared to unphosphorylated ss-siRNA.

Figs. 5A-5C illustrate a model for siRNA-guided mRNA cleavage by Argonaute. (Fig. 5A) Two views of the electrostatic surface potential of PfAgo indicating a positively charged groove suitable for interaction with nucleic acids. The locations of the domains are labeled and the approximate location of the active site in PIWI is marked by a yellow asterisk. The view on the left is slightly tilted on the horizontal axis compared to the view in Figure 1. Two of the loops were removed for a better view of the groove. The binding groove runs horizontally across the protein bending upwards between the PAZ and N-terminal domains on the right and bending around

between the PAZ and middle domains on the left. The view on the right is from the proposed exit groove of the mRNA and looking into the active site area (rotated ~90° compared to the view on the left). The PIWI domain is behind the middle domain in this view. The coloring scheme depicts potentials < -10 k_BT in red and > 10 k_BT in blue, where k_B is the Boltzman constant and T is the absolute temperature. This figure was prepared with GRASP (64).

(Fig. 5B) A model for si-RNA and mRNA binding. Argonaute is shown as a ribbon representation in gray. A 3' portion of the siRNA, shown in purple, was placed by superposition of the PAZ domain of the hAgo1-PAZ domain-RNA complex on the PAZ domain of PfAgo. The two nucleotides at the 3'-end of the siRNA are inserted in the PAZ cleft and the nucleotides 5' to those bind along the PAZ domain. The passenger strand of the hAgo1-PAZ complex placed in a similar manner was used to model the mRNA strand, shown in light blue, by extending the RNA 2 nucleotides at the 5'-end, and from the middle of that strand along the binding groove towards the active site in PIWI. The 5'- end of the mRNA is nested between the PAZ and N-terminal domains, across the stalk. The phosphate between the 11th and 12th nucleotides from the 5'-end of the mRNA falls near the active site residues shown in red.

(Fig. 5C) Schematic depiction of the model for siRNA-guided mRNA cleavage. The domains are colored as in Fig. 1. The siRNA, shown in yellow, binds with its 3'-end in the PAZ cleft and the 5' is predicted to reach the other end of the molecule and likely bind there. The mRNA is depicted in brown, comes in between the N-terminal and PAZ domains and out between the PAZ and middle domain. The active site in the PIWI domain, depicted as scissors, cleaves the mRNA opposite the middle of the siRNA guide.

Fig. 6 shows sequence alignment of the PAZ domains of PfAgo, hAgo1 and DmAgo2 based on the structural superposition of the three domains. The sequence of PfAgo-PAZ domain could not be readily aligned with PAZ domains from other species without knowledge of the structure. Invariant residues are highlighted in purple and conserved residues are highlighted in blue. The secondary structure elements for PfAgo are shown above the sequence.

Fig. 7 shows sequence alignment of the PIWI domains from Pf Argonaute and the four human Argonaute proteins. Invariant residues are highlighted in purple and conserved residues are highlighted in blue. The secondary structure elements are shown above the structure. The conserved active site carboxylate residues are marked by a red asterisk. Accession numbers are as follows: PfAgo (AAL80661), hAgo1 (NM_012199), hAgo2 (NM_012154), hAgo3 (NM_024852) and hAgo4 (NM_017629).

Fig. 8 shows another view of the electrostatic surface potential of PfAgo shown from the proposed exit groove of the mRNA and looking into the active site area (rotated ~90° around y and ~20° around x compared to the in Fig. 4A). The PIWI domain is behind the middle domain in this view.

Fig. 9 shows that only mammalian Ago2 can form cleavage-competent RISC. Panel A: The miRNA populations associated with Ago1, Ago2 and Ago3 were measured by microarray analysis as described in Methods. The heat map shows normalized log-ratio values for each dataset, with yellow representing increased relative amounts, and blue indicating decreased amounts, relative to the median. The top 25 log-ratios are shown in the expanded region. In each panel, "control" indicates parallel analysis of cells transfected with a vector control. Panel B: 293T cells were transfected with a control vector or with vectors encoding myc-tagged Ago1, Ago2 or Ago3, as indicated, along with an siRNA that targets firefly luciferase. Immunoprecipitates were tested for siRNA directed mRNA cleavage as described in Methods. Positions of 5' and 3' cleavage products are shown. Panel C: Immunoprecipitates as in Panel B were tested for in vivo siRNA binding by Northern blotting of Ago immunoprecipitates (see Methods). Panel D: Western blots of transfected cell lysates show similar levels of expression for each recombinant Argonaute protein.

Fig. 10 shows that Argonaute2 is essential for mouse development. Panel A: Total RNA from Wild-type or mutant embryos was tested for expression of Ago1, Ago2 or Ago3 by RT-PCR. Actin was also examined as a control. Panel B: At day E10.5, Ago2 null embryos show severe developmental delay as compared to heterozygous and wild-type littermates. These embryos also show a variety of developmental

defects including swelling inside the pericardial membrane (Panel C, h=heart, indicated by the arrow) and failure to close the neural tube (Panel D, Panel E). Arrows in Panel D indicate the edges of the neural tube that has failed to close. In caudal regions where the neural tube does close, it has an abnormal appearance, being wavy as compared to wild-type embryos (Panel E, compare wt and Ago2 -/-). Ago2 is expressed in most tissues of the developing embyo as measured by in situ hybridization (Panel F) or analysis of an Ago2 gene trap animal (Panel G). In Panel F, f=forebrain, b=branchial arches, h=heart and lb=limb bud, all of which are relative hot spots for Ago2 mRNA. In Panel G, the left embryo shows similar patterns when staining for the gene-trap marker, β-galactosidase, proceeds for only a short period. Longer incubation (Panel G, right) gives uniform staining throughout the embryo.

Fig. 11 shows that Argonaute2 is essential for RNAi in MEF. Panel A: RT-PCR of mRNA prepared from Wild-type or Ago2-/- MEF reveals consistent expression of Ago1 and Ago3 but a specific lack of Ago2 expression in the null MEF. Actin mRNA serves as a control. Panel B: Wild-type and mutant MEFs were co-transfected with plasmids encoding Renilla and firefly luciferases either with or without firefly siRNA as indicated. Ratios of firefly to Renilla activity, normalized to 1 for the no-siRNA control were plotted. For each genotype, the ability of Ago1 and Ago2 to rescue suppression was tested by co-transfection with expression vectors encoding each protein as indicated. Panel C: NIH-3T3 cells, Wild-type MEF or Ago2 mutant MEF were tested as described in B (except that Renilla/firefly ratios are plotted) for their ability to suppress a reporter of repression at the level of protein synthesis. In this case, the Renilla luciferase mRNA contains multiple, imperfect binding sites for a CXCR4 siRNA. Cells were transfected with a mixture of firefly and Renilla luciferase plasmids with or without (as indicated) the siRNA.

Fig. 12 shows mapping of the requirements for assembly of cleavage-competent RISC. Ago1, Ago2 or the indicated mutants of Ago2 were expressed as myc-tagged fusion proteins in 293T cells. In all cases, expression constructs were co-transfected with a luciferase siRNA. Western Blotting (not shown) indicated similar expression for each mutant. Immunoprecipitate containing individual proteins were tested for

cleavage activity against a luciferase mRNA. Positions of 5' and 3' cleavage products are indicated. SiRNA binding was examined for each mutant by Northern blotting of immunoprecipitates or by staining of immunoprecipitates with Sybr Gold (Molecular Probes). Representatives for these assays are shown. In no case was a defect in interaction of mutants with siRNAs detected.

Fig. 13 shows that Argonaute2 is a candidate for Slicer. Panel A: Ago2 protein was immunoaffinity purified from transiently transfected 293T cells. The preparation contained two major proteins (Protein Gel), in addition to heavy and light chains. These were identified by mass spectrometry as Ago2 and HSP90. Immunoprecipitates were mixed (see Methods) in vitro with single- or double-stranded siRNAs or with a 21 nt DNA having the same sequence as the siRNA, as indicated. Reconstituted RISC was tested for cleavage activity with a uniformly labeled synthetic mRNA. Positions of 5' and 3' cleavage products are noted. Where indicated, the siRNA was not 5' phosphorylated and in one case, ATP was not added to the reconstitution reaction. Panel B: Ago2 or Ago2 mutants (as indicated) were assembled into RISC in vivo by co-transfection with siRNAs followed by immunoaffinity purification or by in vitro reconstitution, mixing affinity purified proteins with ss-siRNAs. These were tested for activity against a complementary mRNA substrate. 5' and 3' cleavage products are as in Panel A. Both mutant proteins were expressed at levels similar to wild-type Ago2 and bound siRNAs as readily (Panel C, Panel D) Ago2 (H634P) and (Q633R) behave similarly in this assay.

Fig. 14 shows cleavage by Ago2-containing RISC irrespective of siRNA sequence. Ago2-containing RISCs were formed in vivo by co-transfection. Complexes were recovered by immunoprecipitation and tested for cleavage activity with a uniformly labeled, synthetic mRNA. Positions of 5', and 3' cleavage products expected for each reaction are indicated.

Fig. 15 shows construction of Ago2 mutant mice. The insertional disruption strategy for inactivating mouse Ago2 is shown, along with a southern blot of DNA from wild-type, heterozygous, and null embryos. Probe is indicated by asterisk. For reference, PAZ domain is encoded by exons 5-8. The insertion duplicates exons 3-

6, which includes two exons of the PAZ domain, and inserts ~10 Kb of vector sequences into the gene, creating a high probability that any truncated protein that might be generated from this allele would be non-functional. Additionally, no Ago2 mRNA was detected from these cells by RT-PCR. However, all of the coding capacity of Ago2 does still exist in the mutant genome. Therefore, although all available evidence indicates a null mutation, the possibility cannot be completely ruled out that this mutant can still synthesize a small amount of Ago2, making it a severe hypomorph rather than a null. Southern blots showing the patterns for Wild-type, heterozygous and mutant animals are shown below the disruption strategy.

Fig. 16 shows expression analysis of Ago3 in embryos. Embryonic day 9.5 embryos were collected from timed matings of Wild-type animals. These were stained for expression of Ago3 mRNA by in situ hybridization as described in Methods. Ago3 shows the same expression pattern as is seen in parallel analyses of Ago2 mRNA expression (see Fig. 10, Panel F).

Fig. 17 shows that Ago2-mutant MEF are defective for siRNA-mediated repression WT and Ago2-mutant MEF (genotypes indicated on the left) were transfected with a combination of plasmids encoding dsRed and GFP, either with or without GFP siRNAs (as indictated on the right). Microscopic examination revealed consistent co-expression of dsRed and GFP in the absence of siRNAs in both WT and mutant cells. SiRNAs eliminated co-expression of GFP in WT cells but did not alter GFP expression in Ago2-/- cells.

Fig. 18 shows that intact Ago2 is required for formation of cleavage-competent RISC. Deletions within Ago2 are indicated schematically. Plasmids encoding epitope-tagged versions of each deletion mutant were co-transfected into 293T cells with an siRNA to firefly luciferase. Wild-type Ago2 was similarly expressed as a control. RISCs were immunoaffinity purified and tested for activity against a uniformly labeled mRNA substrate. Each protein was expressed as indicated by Western blotting with a myc antiserum, but none of the deletion mutants bound siRNAs, as determined by Nothern blotting of immunoprecipitates.

Fig. 19 shows that Ago2 can be reconstituted with different siRNAs. Ago2 was immunoaffinitity purified (see Fig. 13) and reconstituted in vitro with single stranded siRNAs that target either the sense strand or the antisense strand of a firefly luciferase mRNA. Similar complexes were formed in parallel with purified Ago1. In each case, Ago2 cleaved the complementary mRNA, whereas Ago1 complexes were inert. Positions of 5', and 3' cleavage products are indicated.

Fig. 20 shows that RISC is a metal-dependent nuclease. As previously shown, RISC requires a divalent metal for activity (Hannon, *supra*). Similarly, RISC, reconstituted in vitro with single-stranded siRNAs, depends on Mg++ for activity, as indicated by the ability to inhibit the complex with EDTA but not with EGTA (as indicated).

Fig. 21 shows that active site residues are conserved among Ago proteins. Putative active site aspartate residues in the PIWI domain were identified with reference to the structure of the *P. furiosus* Ago protein. These were also conserved in Ago proteins from a variety of species. Additionally, residues identified by a mutational analysis (e. g. H634) were also highly conserved.

Fig. 22 shows sequence alignment of mammalian Ago1 family members. An alignment of the protein sequences of human Argonautes1-4 highlights a very high degree of sequence conservation. Red indicates highly conserved, blue moderately conserved residues. Residues mutated in Ago2 in this study are indicated in green and by asterisks (see below). The PAZ domain is indicated by the yellow bar and the PIWI by the orange bar (boundaries set as determined by structural data). Accession numbers for individual genes are as follows: Ago1 (NM_012199), Ago2 (NM_012154), Ago3(NM_024852), Ago4 (NM_017629).

Fig. 23 shows Table 1 which provides crystallographic statistics for Argonaute.

Fig. 24 shows Table 2 which provides additional crystallographic statistics for Argonaute.

Fig. 25 shows Table 3 which provides the atomic coordinates for Argonaute.

DETAILED DESCRIPTION OF THE APPLICATION

Overview

Argonautes are often present as multiprotein families and are identified by two characteristic domains, PAZ and PIWI (21). These proteins mainly segregate into two sub-families, comprising those that are more similar to either Arabidopsis Argonaute1 or Drosophila Piwi. The Argonaute family was first linked to RNAi through genetic studies in C. elegans, which identified Rde-1 as a gene essential for silencing (22). Subsequent placement of a Drosophila Argonaute protein in RISC (19) makes it desirable to explore the unknown roles of this protein family. Toward this end, this application provides methods and compositions related to Argonaute. These methods and compositions are based on results obtained from structural studies of Argonaute proteins, as well as biochemical, and genetic studies of a subfamily of Argonaute proteins in mammals. As used herein, the term "Argonaut" refers to a protein which (a) mediates an RNAi response and (b) has an amino acid sequence at least 50 percent identical, and more preferably at least 75, 85, 90 or 95 percent identical to SEQ ID NOs: 1-5.

Structural Studies of Argonaute

The crystal structure of Argonaute is useful for in silico screening of agents that bind to Argonaute and/or modulates its activity. The candidate agents generated from the in silico screening can be further screened in biochemical assays to select for agents that modulate the activity of Argonaute.

I. Crystallization and Structure Determination

X-ray crystallography is a method of solving the three dimensional structures of molecules. The structure of a molecule is calculated from X-ray diffraction patterns using a crystal as a diffraction grating. Three dimensional structures of protein molecules arise from crystals grown from a concentrated aqueous solution of that protein. The process of X-ray crystallography can include the following steps:

(a) synthesizing and isolating (or otherwise obtaining) a polypeptide;

(b) growing a crystal from an aqueous solution comprising the polypeptide with or without a modulator; and

(c) collecting X-ray diffraction patterns from the crystals, determining unit cell dimensions and symmetry, determining electron density, fitting the amino acid sequence of the polypeptide to the electron density, and refining the structure.

a. Production of Polypeptides

The Argonaute polypeptides described herein may be chemically synthesized in whole or part using techniques that are well-known in the art (see, e.g., Creighton (1983) Biopolymers 22(1):49-58).

Alternatively, methods which are well known to those skilled in the art can be used to construct expression vectors containing the native or mutated Argonaute polypeptide coding sequence and appropriate transcriptional/translational control signals. These methods include in vitro recombinant DNA techniques, synthetic techniques and in vivo recombination/genetic recombination. See, for example, the techniques described in Maniatis, T (1989). Molecular cloning: A laboratory Manual. Cold Spring Harbor Laboratory, New York. Cold Spring Harbor Laboratory Press; and Ausubel, F. M. et al. (1994) Current Protocols in Molecular Biology (John Wiley & Sons, Secaucus, N.J.).

A variety of host-expression vector systems may be utilized to express the Argonaute coding sequence. These include but are not limited to microorganisms such as bacteria transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing the Argonaute domain coding sequence; yeast transformed with recombinant yeast expression vectors containing the Argonaute domain coding sequence; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing the Argonaute domain coding sequence; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti

plasmid) containing the Argonaute domain coding sequence; or animal cell systems. The expression elements of these systems vary in their strength and specificities.

Depending on the host/vector system utilized, any of a number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used in the expression vector. For example, when cloning in bacterial systems, inducible promoters such as pL of bacteriophage .lambda., plac, ptrp, ptac (ptrp-lac hybrid promoter) and the like may be used; when cloning in insect cell systems, promoters such as the baculovirus polyhedrin promoter may be used; when cloning in plant cell systems, promoters derived from the genome of plant cells (e.g., heat shock promoters; the promoter for the small subunit of RUBISCO; the promoter for the chlorophyll alb binding protein) or from plant viruses (e.g., the .sup.35S RNA promoter of CaMV; the coat protein promoter of TMV) may be used; when cloning in mammalian cell systems, promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter) may be used; when generating cell lines that contain multiple copies of the Argonaute domain DNA, SV40-, BPV- and EBV-based vectors may be used with an appropriate selectable marker.

Exemplary methods describing methods of DNA manipulation, vectors, various types of cells used, methods of incorporating the vectors into the cells, expression techniques, protein purification and isolation methods, and protein concentration methods are disclosed in detail in PCT publication WO 96/18738. This publication is incorporated herein by reference in its entirety, including any drawings. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

b. Crystal Growth

Crystals are grown from an aqueous solution containing the purified and concentrated Argonaute polypeptide by a variety of techniques. These techniques include batch, liquid, bridge, dialysis, vapor diffusion, and hanging drop methods. McPherson (1982) John Wiley, New York; McPherson (1990) Eur. J. Biochem.

189:1-23; Webber (1991) Adv. Protein Chem. 41:1-36, incorporated by reference herein in their entireties, including all figures, tables, and drawings.

The native crystals of the application are, in general, grown by adding precipitants to the concentrated solution of the polypeptide. The precipitants are added at a concentration just below that necessary to precipitate the protein. Water is removed by controlled evaporation to produce precipitating conditions, which are maintained until crystal growth ceases.

For crystals of the application, exemplary crystallization conditions are described in the Examples. Those of ordinary skill in the art will recognize that the exemplary crystallization conditions can be varied. Such variations may be used alone or in combination. In addition, other crystallizations may be found, e.g., by using crystallization screening plates to identify such other conditions.

c. X-Ray Diffraction

The diffraction data from X-ray crystallography is generally obtained as follows. When a crystal is placed in an X-ray beam, the incident X-rays interact with the electron cloud of the molecules that make up the crystal, resulting in X-ray scatter. The combination of X-ray scatter with the lattice of the crystal gives rise to nonuniformity of the scatter; areas of high intensity are called diffracted X-rays. The angle at which diffracted beams emerge from the crystal can be computed by treating diffraction as if it were reflection from sets of equivalent, parallel planes of atoms in a crystal (Bragg's Law). The most obvious sets of planes in a crystal lattice are those that are parallel to the faces of the unit cell. These and other sets of planes can be drawn through the lattice points. Each set of planes is identified by three indices, hkl. The h index gives the number of parts into which the a edge of the unit cell is cut, the k index gives the number of parts into which the b edge of the unit cell is cut, and the 1 index gives the number of parts into which the c edge of the unit cell is cut by the set of hkl planes. Thus, for example, the 235 planes cut the a edge of each unit cell into halves, the b edge of each unit cell into thirds, and the c edge of each unit cell into fifths. Planes that are parallel to the bc face of the unit cell are the 100 planes; planes that are parallel to the ac face of the unit cell are the

010 planes; and planes that are parallel to the ab face of the unit cell are the 001 planes.

When a detector is placed in the path of the diffracted X-rays, in effect cutting into the sphere of diffraction, a series of spots, or reflections, are recorded to produce a "still" diffraction pattern. Each reflection is the result of X-rays reflecting off one set of parallel planes, and is characterized by an intensity, which is related to the distribution of molecules in the unit cell, and hkl indices, which correspond to the parallel planes from which the beam producing that spot was reflected. If the crystal is rotated about an axis perpendicular to the X-ray beam, a large number of reflections is recorded on the detector, resulting in a diffraction pattern.

The unit cell dimensions and space group of a crystal can be determined from its diffraction pattern. First, the spacing of reflections is inversely proportional to the lengths of the edges of the unit cell. Therefore, if a diffraction pattern is recorded when the X-ray beam is perpendicular to a face of the unit cell, two of the unit cell dimensions may be deduced from the spacing of the reflections in the x and y directions of the detector, the crystal-to-detector distance, and the wavelength of the X-rays. Those of skill in the art will appreciate that, in order to obtain all three unit cell dimensions, the crystal must be rotated such that the X-ray beam is perpendicular to another face of the unit cell. Second, the angles of a unit cell can be determined by the angles between lines of spots on the diffraction pattern. Third, the absence of certain reflections and the repetitive nature of the diffraction pattern, which may be evident by visual inspection, indicate the internal symmetry, or space group, of the crystal. Therefore, a crystal may be characterized by its unit cell and space group, as well as by its diffraction pattern.

Once the dimensions of the unit cell are determined, the likely number of polypeptides in the asymmetric unit can be deduced from the size of the polypeptide, the density of the average protein, and the typical solvent content of a protein crystal, which is usually in the range of 30-70% of the unit cell volume.

The diffraction pattern is related to the three-dimensional shape of the molecule by a Fourier transform. The process of determining the solution is in

essence a re-focusing of the diffracted X-rays to produce a three-dimensional image of the molecule in the crystal. Since re-focusing of X-rays cannot be done with a lens at this time, it is done via mathematical operations.

The sphere of diffraction has symmetry that depends on the internal symmetry of the crystal, which means that certain orientations of the crystal will produce the same set of reflections. Thus, a crystal with high symmetry has a more repetitive diffraction pattern, and there are fewer unique reflections that need to be recorded in order to have a complete representation of the diffraction. The goal of data collection, a dataset, is a set of consistently measured, indexed intensities for as many reflections as possible. A complete dataset is collected if at least 80%, preferably at least 90%, most preferably at least 95% of unique reflections are recorded. In one embodiment, a complete dataset is collected using one crystal. In another embodiment, a complete dataset is collected using more than one crystal of the same type.

Sources of X-rays include, but are not limited to, a rotating anode X-ray generator such as a Rigaku RU-200 or a beamline at a synchrotron light source, such as the Advanced Photon Source at Argonne National Laboratory. Suitable detectors for recording diffraction patterns include, but are not limited to, X-ray sensitive film, multiwire area detectors, image plates coated with phosphorus, and CCD cameras. Typically, the detector and the X-ray beam remain stationary, so that, in order to record diffraction from different parts of the crystal's sphere of diffraction, the crystal itself is moved via an automated system of moveable circles called a goniostat. The three dimensional (x, y, z) coordinates of Argonaute are shown in Table 3 (Figure 25) in the standard Protein Data Bank (PDB) format. (Bernstain F. C., et al. J. Mol. Biol., 1977, 122, 535).

TABLE 3 –Atomic Coordinates (Figure 25).

Once a dataset such as the one in Table 3 (Figure 25) is collected, the information is used to determine the three-dimensional structure of the molecule in the crystal. However, in the absence alone of a suitable molecular model, this cannot be done from a single measurement of reflection intensities because certain

information, known as phase information, is lost between the three-dimensional shape of the molecule and its Fourier transform, the diffraction pattern. This phase information must be acquired by methods described below in order to perform a Fourier transform on the diffraction pattern to obtain the three-dimensional structure of the molecule in the crystal. It is the determination of phase information that in effect refocuses X-rays to produce the image of the molecule.

One method of obtaining phase information is by isomorphous replacement, in which heavy-atom derivative crystals are used. In this method, the positions of heavy atoms bound to the molecules in the heavy-atom derivative crystal are determined, and this information is then used to obtain the phase information necessary to elucidate the three-dimensional structure of a native crystal. (Blundel et al., 1976, Protein Crystallography, Academic Press).

Another method of obtaining phase information is by molecular replacement, which is a method of calculating initial phases for a new crystal of a polypeptide or polypeptide co-complex whose structure coordinates are unknown by orienting and positioning a related polypeptide whose structure coordinates are known within the unit cell of the new crystal so as to best account for the observed diffraction pattern of the new crystal. To enable this, the related molecule must have a similar three dimensional structure. Briefly, the principle behind the method of molecular replacement is as follows. A suitable search model, whose three-dimensional structure is similar to that of the unknown target, is identified first. The search model is then rotated and translated within the unit cell of the unknown. For each position of the model, a set of structure factors of the model is computed. These calculated structure factors are then compared with the measured intensities of the unknown and expressed as correlation coefficients. The solution with the highest correlation coefficient is selected as the true solution. These concepts are discussed at length in the book "The Molecular Replacement Method edited by Rossmann (1972, Int. Sci. Rev. Ser. No 13, Gordon & Breach, New York).

A third method of phase determination is multi-wavelength anomalous dispersion or MAD. In this method, X-ray diffraction data are collected at several different wavelengths from a single crystal containing at least one heavy atom with

absorption edges near the energy of incoming X-ray radiation. The resonance between X-rays and electron orbitals leads to differences in X-ray scattering that permits the locations of the heavy atoms to be identified, which in turn provides phase information for a crystal of a polypeptide. A detailed discussion of MAD analysis can be found in Hendrickson, 1985, Trans. Am. Crystallogr. Assoc., 21:11; Hendrickson et al., 1990, EMBO J. 9:1665; and Hendrickson, 1991, Science 4:91.

A fourth method of determining phase information is single wavelength anomalous w dispersion or SAD. In this technique, X-ray diffraction data are collected at a single wavelength from a single native or heavy-atom derivative crystal, and phase information is extracted using anomalous scattering information from atoms such as sulfur or chlorine in the native crystal or from the heavy atoms in the heavy-atom derivative crystal. A detailed discussion of SAD analysis can be found in Brodersen et al., 2000, Acta Cryst., D56:431-441.

A fifth method of determining phase information is single isomorphous replacement with anomalous scattering or SIRAS. This technique combines isomorphous replacement and anomalous scattering techniques to provide phase information for a crystal of a polypeptide. X-ray diffraction data are collected at a single wavelength, usually from a single heavy-atom derivative crystal. Phase information obtained only from the location of the heavy atoms in a single heavy-atom derivative crystal leads to an ambiguity in the phase angle, which is resolved using anomalous scattering from the heavy atoms. Phase information is therefore extracted from both the location of the heavy atoms and from anomalous scattering of the heavy atoms. A detailed discussion of SIRAS analysis can be found in North, 1965, Acta Cryst. 18:212-216; Matthews, 1966, Acta Cryst. 20:82-86.

Once phase information is obtained, it is combined with the diffraction data to produce an electron density map, an image of the electron clouds that surround the molecules in the unit cell. The higher the resolution of the data, the more distinguishable are the features of the electron density map, e.g., amino acid side chains and the positions of carbonyl oxygen atoms in the peptide backbones, because atoms that are closer together are resolvable. A model of the macromolecule is then built into the electron density map with the aid of a computer,

using as a guide all available information, such as the polypeptide sequence and the established rules of molecular structure and stereochemistry. Interpreting the electron density map is a process of finding the chemically realistic conformation that fits the map precisely.

After a model is generated, the structure is refined. Refinement is the process of minimizing the function Φ, which is the difference between observed and calculated intensity values (measured by an R-factor), and which is a function of the position, temperature factor, and occupancy of each non-hydrogen atom in the model. This usually involves alternate cycles of real space refinement, i.e., calculation of electron density maps and model building, and reciprocal space refinement, i.e., computational attempts to improve the agreement between the original intensity data and intensity data generated from each successive model. Refinement ends when the function Φ converges on a minimum wherein the model fits the electron density map and is stereochemically and conformationally reasonable. During refinement, ordered solvent molecules are added to the structure.

d. Various representations

The atomic structure coordinates and machine readable media of the application have a variety of uses. The present invention encompasses the structure coordinates and other information, e.g., amino acid sequence, connectivity tables, vector-based representations, temperature factors, etc., used to generate the three-dimensional structures of the polypeptides for use in the software programs described below and other software programs. For example, the coordinates listed in Table 3 (Figure 25) are useful for solving the three-dimensional crystal or solution structures of other proteins to high resolution.

Additionally, the invention encompasses machine readable media embedded with the three-dimensional structures of the models described herein, or with portions thereof. As used herein, "machine readable medium" or "computer readable medium" refers to any medium that can be read and accessed directly by a computer or scanner. Such media include, but are not limited to: magnetic storage

media, such as floppy discs, hard disc storage medium and magnetic tape; optical storage media such as optical discs or CD-ROM; electrical storage media such as RAM or ROM; and hybrids of these categories such as magnetic/optical storage media. Such media further include paper on which is recorded a representation of the atomic structure coordinates, e.g., Cartesian coordinates, that can be read by a scanning device and converted into a three-dimensional structure with an Optical Character Recognition (OCR).

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon the atomic structure coordinates of the application or portions thereof and/or X-ray diffraction data. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the sequence and X-ray data information on a computer readable medium. Such formats include, but are not limited to, Protein Data Bank ("PDB") format (Research Collaboratory for Structural Bioinformatics; http://www.rcsb.org/pdb/docs/format/pdbguide2.2/guide2.2_frame.html); Cambridge Crystallographic Data Centre format (http://www.ccdc.cam.ac.uk/support/csd_doc/volume3/z323.html); Structure-data ("SD") file format (MDL Information Systems, Inc.; Dalby et al., 1992, J. Chem. Inf. Comp. Sci. 32:244-255), and line-notation, e.g., as used in SMILES (Weininger, 1988, J. Chem. Inf. Comp. Sci. 28:31-36). Methods of converting between various formats read by different computer software will be readily apparent to those of skill in the art, e.g., BABEL (v. 1.06, Walters & Stahl, © 1992, 1993, 1994; http://www.brunel.ac.uk/departments/chem/babel.htm.) All format representations of the polypeptide coordinates described herein, or portions thereof, are contemplated by the present invention. By providing computer readable medium having stored thereon the atomic coordinates of the application, one of skill in the art can routinely access the atomic coordinates of the application, or portions thereof, and related information for use in modeling and design programs, described in detail below.

While Cartesian coordinates are important and convenient representations of the three-dimensional structure of a polypeptide, those of skill in the art will readily recognize that other representations of the structure are also useful. Therefore, the three-dimensional structure of a polypeptide, as discussed herein, includes not only the Cartesian coordinate representation, but also all alternative representations of the three-dimensional distribution of atoms. For example, atomic coordinates may be represented as a Z-matrix, wherein a first atom of the protein is chosen, a second atom is placed at a defined distance from the first atom, a third atom is placed at a defined distance from the second atom so that it makes a defined angle with the first atom. Each subsequent atom is placed at a defined distance from a previously placed atom with a specified angle with respect to the third atom, and at a specified torsion angle with respect to a fourth atom. Atomic coordinates may also be represented as a Patterson function, wherein all interatomic vectors are drawn and are then placed with their tails at the origin. This representation is particularly useful for locating heavy atoms in a unit cell. In addition, atomic coordinates may be represented as a series of vectors having magnitude and direction and drawn from a chosen origin to each atom in the polypeptide structure. Furthermore, the positions of atoms in a three-dimensional structure may be represented as fractions of the unit cell (fractional coordinates), or in spherical polar coordinates.

Additional information, such as thermal parameters, which measure the motion of each atom in the structure, chain identifiers, which identify the particular chain of a multi-chain protein or protein co-complex in which an atom is located, and connectivity information, which indicates to which atoms a particular atom is bonded, is also useful for representing a three-dimensional molecular structure.

e. Structure of Argonaute

The present invention provides high-resolution three-dimensional structures and atomic structure coordinates of crystalline Argonaute as determined by X-ray crystallography. The specific methods used to obtain the structure coordinates are provided in the examples and throughout the application. The atomic structure coordinates of crystalline Argonaute are listed in Table 3 (Figure 25).

Those having skill in the art will recognize that atomic structure coordinates as determined by X-ray crystallography are not without error. Thus, it is to be understood that any set of structure coordinates obtained for crystals of Argonaute, whether native crystals, derivative crystals or co-crystals, that have a root mean square deviation ("r.m.s.d.") of less than or equal to about 1.5 Angstrom when superimposed, using backbone atoms (N, Cα, C and O), on the structure coordinates listed in Table 3 (Figure 25) are considered to be identical with the structure coordinates listed in the Table 3 (Figure 25) when at least about 50% to 100% of the backbone atoms of Argonaute are included in the superposition.

II. Crystalline Argonaute

It is to be understood that the crystalline Argonaute of the application are not limited to naturally occurring or native Argonaute. Indeed, the crystals of the application include crystals of mutants of native Argonaute. Mutants of naturally-occurring or native Argonautes are obtained by replacing at least one amino acid residue in a native Argonaute with a different amino acid residue, or by adding or deleting amino acid residues within the native polypeptide or at the N- or C-terminus of the native polypeptide, and have substantially the same three-dimensional structure as the native Argonaute from which the mutant is derived.

By having substantially the same three-dimensional structure is meant having a set of atomic structure coordinates that have a root-mean-square deviation of less than or equal to about 2 angstrom when superimposed with the atomic structure coordinates of the native Argonaute from which the mutant is derived when at least about 50% to 100% of the Ca atoms of the native Argonaute domain are included in the superposition.

Amino acid substitutions, deletions and additions which do not significantly interfere with the three-dimensional structure of the Argonaute will depend, in part, on the region of the Argonaute where the substitution, addition or deletion occurs. In highly variable regions of the molecule, non-conservative substitutions as well as conservative substitutions may be tolerated without significantly disrupting the three-dimensional, structure of the molecule. In highly conserved regions, or

regions containing significant secondary structure, conservative amino acid substitutions are preferred.

Conservative amino acid substitutions are well known in the art, and include substitutions made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the amino acid residues involved. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; amino acids with uncharged polar head groups having similar hydrophilicity values include the following: leucine, isoleucine, valine; glycine, alanine; asparagine, glutamine; serine, threonine; phenylalanine, tyrosine. Other conservative amino acid substitutions are well known in the art.

For Argonaute obtained in whole or in part by chemical synthesis, the selection of amino acids available for substitution or addition is not limited to the genetically encoded amino acids. Indeed, the mutants described herein may contain non-genetically encoded amino acids. Conservative amino acid substitutions for many of the commonly known non-genetically encoded amino acids are well known in the art. Conservative substitutions for other amino acids can be determined based on their physical properties as compared to the properties of the genetically encoded amino acids.

In some instances, it may be particularly advantageous or convenient to substitute, delete and/or add amino acid residues to a native Argonaute in order to provide convenient cloning sites in cDNA encoding the polypeptide, to aid in purification of the polypeptide, and for crystallization of the polypeptide. Such substitutions, deletions and/or additions which do not substantially alter the three dimensional structure of the native Argonaute domain will be apparent to those of ordinary skill in the art.

It should be noted that the mutants contemplated herein need not all exhibit Argonaute activity. Indeed, amino acid substitutions, additions or deletions that interfere with the Argonaute activity but which do not significantly alter the three-dimensional structure of the domain are specifically contemplated by the invention.

Such crystalline polypeptides, or the atomic structure coordinates obtained therefrom, can be used to identify compounds that bind to the native domain. These compounds can affect the activity of the native domain.

The co-crystals of the application generally comprise a crystalline Argonaute domain polypeptide in association with one or more compounds. The association may be covalent or non-covalent. Such compounds include, but are not limited to, cofactors, substrates, substrate analogues, modulators, allosteric effectors, etc.

Argonaute

As used herein, the term "Argonaut" refers to a protein which (a) mediates an RNAi response and (b) has an amino acid sequence at least 50 percent identical, and more preferably at least 75, 85, 90 or 95 percent identical to SEQ ID NOs.: 1-5.

Mammals contain four Argonaute1 subfamily members, Ago1-Ago4 (nomenclature as in (Carmell et al., Genes Dev. 16, 2733 (2002)), see Fig. 22 which provides sequence alignment of human Ago1-4 proteins, corresponding to SEQ ID NOs: 1-4). Different Argonaute family members in Drosophila preferentially associate with different small RNAs, with Ago1 preferring miRNAs and Ago2 siRNAs (24). Recent studies of dmAgo1 and dmAgo2 mutants have strengthened these conclusions (25). To assess whether mammalian Ago proteins specialized in their interactions with small RNAs, Ago-associated miRNA populations were examined by microarray analysis (Example 1).

Amino Acid Sequence of *Pyrococcus furiosus* Argonaute Protein:

SEQ ID NO.: 5

MKAKVVINLVKINKKIIPDKIYVYRLFNDPEEELQKEGYSIYRLAYEN
VGIVIDPENLIIATTKELEYEGEFIPEGEISFSELRNDYQSKLVLRLLKENGIGE
YELSKLLRKFRKPKTFGDYKVIPSVEMSVIKHDEDFYLVIHIIHQIQSMKTLW
ELVNKDPKELEEFLMTHKENLMLKDIASPLKTVYKPCFEEYTKKPKLDHNQ
EIVKYWYNYHIERYWNTPEAKLEFYRKFGQVDLKQPAILAKFASKIKKNKN
YKIYLLPQLVVPTYNAEQLESDVAKEILEYTKLMPEERKELLENILAEVDSDI

IDKSLSEIEVEKIAQELENKIRVRDDKGNSVPISQLNVQKSQLLLWTNYSRKY
PVILPYEVPEKFRKIREIPMFIILDSGLLADIQNFATNEFRELVKSMYYSLAKK
YNSLAKKARSTNEIGLPFLDFRGKEKVITEDLNSDKGIIEVVEQVSSFMKGKE
LGLAFIAARNKLSSEKFEEIKRRLFNLNVISQVVNEDTLKNKRDKYDRNRLD
LFVRHNLLFQVLSKLGVKYYVLDYRFNYDYIIGIDVAPMKRSEGYIGGSAV
MFDSQGYIRKIVPIKIGEQRGESVDMNEFFKEMVDKFKEFNIKLDNKKILLLR
DGRITNNEEEGLKYISEMFDIEVVTMDVIKNHPVRAFANMKMYFNLGGAIY
LIPHKLKQAKGTPIPIKLAKKRIIKNGKVEKQSITRQDVLDIFILTRLNYGSISA
DMRLPAPVHYAHKFANAIRNEWKIKEEFLAEGFLYFV

1. Overall Architecture

This application provides the structure of the full-length Argonaute from the archaebacterium *Pyrococcus furiosus* (PfAgo) as determined by x-ray crystallography to 2.25 Å resolution. The structure was solved by multiple anomalous dispersion (MAD) and isomorphous replacement using selenium and mercury derivatives (Table 2 shown in Figure 24)). The N-terminal, middle, and PIWI domains form a crescent-shaped base, with the PIWI domain at the center of the crescent. The region following the N-terminus forms a "stalk" that holds the PAZ domain above the crescent and an interdomain connector cradles the molecule (Fig. 1). This architecture results in a cleft formed at the center of the crescent with the PAZ domain closing in on this cleft.

The N-terminal domain consists of a long strand at the bottom of the crescent, continuing to a region of a small four-stranded β-sheet, three α-helices and a β-hairpin, which then extends to the three-stranded antiparallel β-sheet stalk.

Also provided is the PAZ domain, a globular domain that adopts an OB-like β-barrel fold with an attachment on one side of the barrel and a cleft in between. This cleft was shown to be the binding site for the 2-nucleotide 3'-overhang of the siRNA (29, 32, 33) and is angled towards the crescent. The PAZ domain in PfAgo superimposes very well with the PAZ domains from Drosophila Argonaute 1 (30) and 2 (29, 31) and with the human Argonaute-1 (hAgo1) PAZ domain in complex

with a "mini-siRNA" (33), though the attachment in the archael protein has two α-helices rather than an α-helix and a β-hairpin (Figs. 2A and 2B).

The middle domain, which is located at one end of the crescent, is an α/β open sheet domain composed of a central three-stranded parallel β-sheet surrounded by α-helices. This domain is similar to the glucose-galactose-arabinose-ribose binding protein family and is most similar to Lac repressor (35). The middle domain also has small three-stranded β-sheet on the outer surface of the crescent, connecting it to the rest of the molecule.

Further provided is the PIWI domain, which is at the C-terminus of Argonaute (residues 545-770). It sits in the middle of the crescent and below the PAZ domain. The crystal structure reveals the presence of a prominent central five-stranded β-sheet flanked on both sides by α-helices at the core of the PIWI domain. A smaller β-sheet extends from the central β-sheet and attaches PIWI to the N-terminal domain and to portions of the interdomain connector.

2. Domain Structure

As mentioned above, the PAZ domain superimposes very well with all the other PAZ domains with known structures, namely, Drosophila Argonautes 1 and 2 and hAgo1 (Fig. 2A). Most of the differences lie in loop regions. The root-mean-square deviation (rmsd) between hAgo1-PAZ and the PAZ domain in this structure is approximately 1.4 Å (for 53 Ca's). Though it is now possible to align the sequence of the PAZ domain of PfAgo with PAZ domains from Argonaute proteins of higher eukaryotes (Fig. 2B) based on the structures, homologies between the archeal and eukaryotic PAZ domains was not apparent before the PfAgo structure was determined. In fact, primary sequence comparisons provided no evidence that PfAgo contained a PAZ domain. Even after attempting to align the sequences with reference to the three-dimensional structures, the sequence identity remains below 10%. The presence and location of the PIWI domain was, on the other hand, obvious from the primary sequence, and could be readily identified through BLAST searches.

The role of the PAZ domain, as shown for fly Ago-2 (29, 32) and for hAgo-1 (33) is to bind the 2-nucleotide 3' overhang of the siRNA. Importantly, the conserved aromatic residues that fill the cleft and were shown to bind those nucleotides (29, 32, 33) are all present in the PfAgo PAZ domain. Curiously, in some cases, these side chains occupy similar positions in space even if they aren't anchored to positions on the peptide backbone corresponding to those in eukaryotic proteins. Specifically, Y212, Y216, H217 and Y190 are equivalent to Y309, Y314, H269 and Y277 of hAgo1 that were shown to bind the oxygens of the phosphate that links the two bases in the overhang. Residue Y190 of PfAgo superimposes perfectly on hAgo1-Y277 that was also shown to bind the 2'-hydroxyl of the penultimate nucleotide. Residues L263 and I261 can assume the role of L337 and T335, which anchor the sugar ring of the terminal residue through van der Waals interactions in the hAgo1-RNA structure. There is an aromatic residue, F292 in hAgo1 that stacks against the terminal nucleotide. This position is occupied by another aromatic, W213, in PfAgo. Finally, R220 in the structure of the present application is positioned similarly to K313 that contacts the penultimate nucleotide. As for residues that were shown to bind the region of the RNA strand 5' to the overhang, K191 is positioned as R278 in hAgo1 to bind phosphates and Y259 is equivalent to K333. Other PAZ residues, such as K252, K248, Q276 and N176 are probably used to bind that strand as well. Accordingly, the PAZ domain in PfAgo appears to have a similar function to the PAZ domains of the fly and human Argonautes and would also be capable of binding a 3' single-stranded region of an RNA molecule.

The present application also provides a PIWI domain core having a tertiary structure that belongs to the RNase H family of enzymes, which include RNase H type 1 and type 2 enzymes. This fold is also characteristic of other enzymes with nuclease or polynucleotidyl transferase activities, such as HIV and ASV integrases (36, 37), RuvC (38), a Holliday junction endonuclease, and transposases such as Mu (39) and Tn5 (40). The closest matches, however, are with RNase HII (41) and RNase H1 (42). The rmsd's between these proteins and PfAgo are of 1.9 Å and they are topologically identical (Fig. 3A). RNase H fold proteins all have a five-stranded mixed β-sheet surrounded by helices. In the RNase H enzymes as well as PIWI, there are two helices on either side of the β-sheet. On one side these are very

similar, and on the other, one of the helices varies. PIWI has an insertion between the last strand and the last helix of the RNase H fold. This insertion consists of a smaller β-sheet attachment and a helix that links it to the rest of the protein. RNase HII has a cap domain that sits above the active site cleft and forms a groove for substrate binding (43). In addition, several residues from the cap domain appear to participate in substrate recognition. The positioning of the cap relative to the RNase H fold of the protein is approximately the same as the PAZ domain relative to the PIWI domain in Argonaute.

Similarity is not restricted to the protein fold. In all of these enzymes there are three highly conserved carboxylates which are essential for catalytic activity (44). Two of these carboxylate side chains are always located on the first strand, β1, which is the central strand of the β-sheet, and at the C-terminus of the fourth strand, β4, of the RNase H fold, which is adjacent to β1 (the red and green strands in Figs. 3A and 3B). The position of the third carboxylate varies between the different RNase H fold enzymes. Remarkably, when examining a superposition between either RNase H1 or RNase HII and PIWI, two aspartate residues were located at the same positions as the invariant carboxylates of the RNase H fold (Fig. 3B). These are D558 located on the first b-strand of PIWI and D628 located at the end of the fourth strand of the PIWI domain. These aspartates are equivalent to D10 and D70 in *E. coli* RNase H1, D7 and D112 in *Methanococcus jannaschii* RNase HII, and D6 and D101 in *Archaeoglobus fulgidus* RNase HII. The location of the third carboxylate, a glutamate, in RNase H1 and HII is occupied by a valine in Argonaute. However, a glutamate, E635, is in close proximity to the two aspartates, and this glutamate may serve as the third active site residue. This residue is positioned on the second helix of the RNase H fold of PIWI (the blue helix in Figs. 3A-3B). Since the position of the third carboxylate varies in these proteins, the only requirement would be for a reasonable spatial position at the active site, a criterion which E635 meets. Therefore, the active site of PfAgo is likely composed of the carboxylate triad formed by D528, D628 and E635 that make up the "DDE" motif. Interestingly, an arginine, R627, is also positioned at the center of the active site, as in the case of the IS4 family of transposases such as Tn5 which appear to have a "DDRE motif"

(40, 45). The active site is thus positioned in a cleft in the middle of the crescent in the groove below the PAZ domain.

RNase H enzymes as well as other polynucleotidyl transferase enzymes require the presence of divalent metal ions for activity. However, the precise role of the metal ions remains unclear. Both one and two metal ion mechanisms have been proposed. *E. coli* RNase H1 is thought to work via a one-metal ion mechanism in which Mg^{2+}, coordinated by one carboxylate group, mediates interactions with the nucleic acid substrate. The other two carboxylates activate a water molecule that can then attack the scissile phosphate bond (46, 47). The two-metal ion mechanism was first proposed for the 3' to 5' exonuclease of the Klenow fragment (48, 49). In this case, one metal interacts with the substrate and stabilizes the reaction intermediate and the other activates a water molecule and positions it to attack the scissile phosphate. Indeed, only one metal is observed in the crystal structures of *E. coli* RNase H1 (42) and *A. fulgidus* RNase HII (43) while two are seen in the active site of the isolated HIV RNase H domain of reverse transcriptase (50). Though the absence of a second metal ion in a crystal structure does not preclude a two-metal ion mechanism (since the second metal may have weak binding in the absence of substrates) there are indications that RNase H1 does use a single-metal ion mechanism while HIV RNase H uses two (51). For the PIWI domain of PfAgo, a strong peak is identified in the F_{obs}-F_{calc} difference electron density map near D558, and it is assigned as a water molecule at this time. By growing crystals in the presence of divalent metal ions, this may be assigned as a metal site unambiguously. A divalent metal ion appears to be required for Argonaute activity (52, 53).

3. siRNA Binding

The role of Argonaute is presently unknown in archaebacteria. Because of its similarity to Argonautes in eukaryotes, the siRNA binding characteristics of PfAgo were examined by using crosslinking and competition assays. A single-stranded 21-mer siRNA containing an IodoU nucleotide to facilitate crosslinking gave rise to a crosslinked species, whereas a double-stranded siRNA did not (Fig. 4A). In addition, the same labeled ss-siRNA can be readily competed off with an identical unlabeled oligonucleotide. However, a similar ss-siRNA lacking the 5'-

phosphate moiety was unable to compete for crosslinking, even at greater than ten-fold the concentration than that at which competition with the 5'-phosphorylated ss-siRNA was seen (Fig. 4B). Thus, there appears to be a requirement for a bona fide siRNA for binding. Preferential binding of the ss-siRNA over the ds-version is consistent with the observation that a ds-siRNA cannot be loaded in vitro to an RISC complex, though an ss-siRNA can be. Accordingly, the present application provides an RISC complex comprising an RNAi construct, e.g., an ss-siRNA. The RISC complex preferably comprises an Argonaute protein, most preferably, an Argonaute protein with the "slicer" activity, described in greater detail below.

4. "Slicer" Activity

The finding that the PIWI domain in Argonaute is an RNase H domain suggests Argonaute as the, as of yet unidentified, "Slicer" enzyme of RISC, that is, the enzyme that cleaves the mRNA. RNase H enzymes specialize in single-stranded cleavage of RNA "guided" by a DNA strand in a double-stranded RNA/DNA hybrid. In a similar manner, Argonautes may specialize in RNA cleavage, in particular mRNA, guided by the siRNA strand in a ds RNA substrate. Moreover, unlike most RNases that leave a 3'-phosphate and 5'-OH, RNase H enzymes produce products with 3'-OH and 5' phosphate groups (54). Recently, Martinez and Tuschl, and Zamore and colleagues showed that cleavage of the mRNA by RISC produces the latter type of termini (52, 53). A dependence on Mg^{2+} for activity is another hallmark of RNase H enzymes and RISC was also shown to require Mg^{2+} for cleavage as well (52). The PAZ domain, shown to recognize and bind the 3' ends of siRNAs, and the PIWI domain, now shown to be an RNase H domain for catalytic activity, combine the necessary features of the slicing component of the RNAi machinery. Therefore, Argonaute, the signature component of RISC, can be "Slicer" itself.

5. A Model for si-RNA-Guided mRNA Cleavage

The placement of the PAZ domain on top of the crescent formed by the N-terminal, middle and PIWI domains and cradled by the connecter region in the structure of Argonaute defines a distinct groove through the protein. The groove has

a claw shape that bends around between the PAZ and N-terminal domains. A striking feature of the structure is evident when the electrostatic potential is mapped on the surface of the protein. As shown in Fig. 5A, the surface of this inner groove is completely lined with positive charges. These positive charges are of course suitable for interaction with the negatively charged phosphate backbone and with the 2'-hydroxyl moieties of an RNA molecule, implicating the groove for substrate binding. The substrate for Argonaute is a ds-RNA molecule composed of an ss-siRNA acting as a guide and the mRNA.

In order to examine possible substrate binding modes for Argonaute, the knowledge of siRNA binding to the PAZ domain using the known PAZ-RNA structure (33) and the mode of binding of RNase H substrates (43, 55-57) were combined. Since the PAZ domain of PfAgo superimposes so well with the PAZ domain of hAgo1 in the PAZ-RNA complex as shown above, the two PAZ domains were superimposed and examined for the resulting position of the RNA with respect to PfAgo. The strand that interacts with its 3' end in the PAZ cleft was regarded as the siRNA guide. The second strand would then be regarded as the mRNA substrate strand (see Fig. 5B). The siRNA guide has its 2 nucleotides at its 3' end inserted into the PAZ cleft. The nucleotides just 5' to that track the top of the PAZ b-barrel making very similar, if not identical, interactions with the PAZ domain as in the crystal structure of the PAZ-RNA complex. A long loop present in the PfAgo PAZ domain would probably move up slightly to accommodate the siRNA. Upon examination of the resulting location of the passenger strand, the mRNA would be coming into the binding groove with its 5' end between the PAZ and the N- terminal domains. The N-terminus then acts as an "mRNA grip" on that end of the molecule. It should be noted that there is another extension of the groove that lies between the N-terminal and the PIWI domains, which could accommodate a single-stranded nucleic acid.

The double-stranded RNA was further extended into the molecule along the binding groove by model building. Remarkably, the mRNA would be positioned above the active site located in the PIWI domain 9 nucleotides from the 5'-side end of the double-stranded region, or rather 11 nucleotides if the 2 nucleotides of the

guide that are inserted into the PAZ domain are counted and are probably not interacting with the mRNA. In other words, the scissile bond would be predicted to be between nucleotides 11 and 12 from the 5' end of the message or from the 3'-end of the guide. This precisely coincides with the demonstrated cleavage of mRNAs by RISC 10 nucleotides from the 5' end of an siRNA. The remainder of the RNA would then continue along the binding groove (Fig. 5C). The interdomain connecter is also forming part of the back wall of the binding groove. As the RNA molecule would have to bend somewhat, the details of some of these interactions are not clear. However, the length of the groove appears to accommodate the length of the siRNA guide, with the 5' end of the guide probably interacting with the other side of the groove. From studies of other RNase H enzymes, Argonaute may sense the minor groove width of the dsRNA, which is different from that of dsDNA and from the minor groove width of a RNA/DNA hybrid, and which is in accord with the inability of RISC to cut DNA substrates (53). This mode of recognition would be in addition to binding the 3' end of the siRNA and sensing the phosphate at the 5'end, as shown in the binding experiments (Fig. 4).

The groove as observed in the crystal structure presented here, in the absence of substrate, would fit an A-RNA double helix snugly. Though a single-stranded RNA should bind fairly readily, opening the claw of the molecule somewhat might assist binding the mRNA, after which it can close down on the double stranded substrate. A hinge region may exist in the interdomain connector at residues 317-320. This hinge could lift the PAZ and the away from the crescent base. This is reasonable since a RISC loading complex appears to be required for assembling an active RISC (58, 59).

The notion that RISC "Slicer" activity, i.e. siRNA-guided mRNA cleavage, resides in Argonaute itself was tested in a mammalian system where the RNAi pathway is known to function. It appears that mammalian Argonaute proteins are distinct and that Ago2 is functional for mRNA cleavage. Based on the sequence alignment with the archael protein, D597, D669 and a third amino acid (e.g., E683) of hAgo2 correspond to D558, D628 and E635 of PfAgo to form the catalytic triad "DDE" motif. There is an insertion near E683, and E673 may also act as the third

carboxylate in hAgo2. The conserved active site aspartates were mutated and the mutants lost their nuclease activity while retaining binding to the siRNA guide. Therefore, Argonaute itself functions as the Slicer enzyme in the RNAi pathway.

In siRNA-guided mRNA cleavage, once RISC is formed, it needs to identify its homologous targets, both for target cleavage and for repression at the level of protein synthesis. In the latter case, there is a presumably stable interaction that occurs between the siRNA and its target, with the target being somehow protected from cleavage. Certainly, an absence of base pairing in the region of the active site might distort the complex sufficiently to prevent catalysis.

Furthermore, several Argonaute protein family members appear to be inactive towards mRNA cleavage despite the presence of the catalytic residues. The basis for these differences may help elucidate the details of the mechanism for siRNA-guided mRNA cleavage. The situation here might be somewhat analogous to the case of the transposase Tn5 and its inhibitor, which posses a catalytic domain with a similar RNase H-like fold. Tn5 inhibitor is a truncated version of the active Tn5 transposase and retains the essential catalytic residues. However, there are major conformational differences between the two that result in domains of the proteins being in different positions relative to one another (40, 45). Similarly, mutations have been introduced into a catalytically active Ago protein, hAgo2, in the vicinity of the active site, which change residues to corresponding residues in an inactive Ago, hAgo1. These inactivate Ago2 for cleavage, indicating that there are determinants for catalysis beyond simply the catalytic triad and that relatively minor alterations in the PIWI domain can have profound effects on its activity toward RNA substrates. The common fold in the catalytic domain of Argonaute family members and transposases and integrases is also intriguing given the relationship of RNAi with control of transposition. It is worth noting that the identification of the catalytic center of RISC awaited a drive toward understanding RNAi at a structural level. Thus, it seems likely that, as in the present example, a full understanding of the underlying mechanism of RNAi will derive from a combination of detailed biochemical and structural studies of RISC.

Assays

The assays and methods described herein may used in combination or separately. For example, an in silico screening and an in vitro binding assay and/or an activity assay may be combined to identify a binding agent and/or a binding agent for a protein that also modulates activity of the protein.

I. Assays Based on the Atomic Structure Coordinates

Structural information, often in the form of atomic structure coordinates, may also be used in a variety of molecular modeling and computer-based screening applications to, for example, design variants that have altered biological properties or to computationally design, screen for and/or identify compounds that bind to the Argonaute protein or to fragments of the Argonaute protein. These compounds may modulate the activity of Argonaute protein and hence the RISC activity.

Thus, in a further aspect of the application, the data from the crystal structure of Argonaute is used to evaluate compounds for their utility as modulators of Argonuate protein. These methods comprise designing and synthesizing candidate compounds using the atomic coordinates of the three dimensional structure of such co-crystals and screening for its utility in various pharmaceutical applications.

In another embodiment, the structures are probed with a plurality of molecules to determine their ability to bind to the Argonaute protein at various sites. Such molecules may be able to modulate the activity of Argonaute protein.

In yet another embodiment, the structures can be used to computationally screen small molecule databases for chemical entities or compounds that can bind in whole, or in part, to Argonaute. In this screening, the quality of fit of such entities or compounds to the binding site may be judged either by shape complementarity or by estimated interaction energy. (Meng et al., 1992, J. Comp. Chem. 13:505-524).

The design of compounds that bind to Argonaute according to this invention generally involves consideration of two factors. First, the compound must be capable of physically and structurally associating with Argonaute. This association

can be covalent or non-covalent. For example, covalent interactions may be important for designing suicide or irreversible inhibitors of a protein. Non-covalent molecular interactions important in the association of Argonaute include hydrogen bonding, ionic and other polar interactions, interactions as well as van der Waals interactions. Second, the compound must be able to assume a conformation that allows it to associate with the Argonaute protein. Although certain portions of the compound will not directly participate in this association with the protein, those portions may still influence the overall conformation of the molecule. This, in turn, may have a significant impact on potency. Such conformational requirements include the overall three-dimensional structure and orientation of the chemical group or compound in relation to all or a portion of the binding site, or the spacing between functional groups of a compound comprising several chemical groups that directly interact with the protein.

The potential modulatory or binding effect of a chemical compound on Argonaute may be analyzed prior to its actual synthesis and testing by the use of computer modeling techniques. If the theoretical structure of the given compound suggests insufficient interaction and association between it and the protein, synthesis and testing of the compound is unnecessary. However, if computer modeling indicates a strong interaction, the molecule may then be synthesized and tested for its ability to bind to the protein and inhibit its activity. In this manner, synthesis of ineffective compounds may be avoided.

A binding compound of Argonaute may be computationally evaluated and designed by means of a series of steps in which chemical groups or fragments are screened and selected for their ability to associate with the individual binding pockets or interface surfaces of each of the proteins. One skilled in the art may use one of several methods to screen chemical groups or fragments for their ability to associate with Argonaute. Docking may be accomplished using software such as QUANTA and SYBYL, followed by energy minimization and molecular dynamics with standard molecular mechanics force fields, such as CHARMM and AMBER.

Specialized computer programs may also assist in the process of selecting fragments or chemical groups. These include:

1. GRID (Goodford, 1985, J. Med. Chem. 28:849-857). GRID is available from Oxford University, Oxford, UK;

2. MCSS (Miranker & Karplus, 1991, Proteins: Structure, Function and Genetics 11:29-34). MCSS is available from Molecular Simulations, Burlington, Mass.;

3. AUTODOCK (Goodsell & Olsen, 1990, Proteins: Structure, Function, and Genetics 8:195-202). AUTODOCK is available from Scripps Research Institute, La Jolla, Calif.;

4. DOCK (Kuntz et al., 1982, J. Mol. Biol. 161:269-288). DOCK is available from University of California, San Francisco, Calif.;

5. FlexE (Clausen H, Buning C, Rarey M and Lengauer T) J. Mol. Biol. (2001) 308, 377-395. FlexE is available from Tripos, St. Louis, Mo.;

6. Glide, Glide is available from Schrodinger, Portland, Oreg.;

7. Gold, Jones et al. J. Mol. Biol. 245, 43-53, 1995;

8. QXP, McMartin C, Bohacek RS. J Comput Aided Mol Des 1997 11:333-44;

9. ICM. (http://www.molsoft.com). Available from Molsoft, San Diego, Calif.; and

10. FlexX. [Sybl, Tripos, St. Louis, Mo

Once suitable chemical groups or fragments have been selected, they can be assembled into a single compound. Assembly may proceed by visual inspection of the relationship of the fragments to each other in the three-dimensional image displayed on a computer screen in relation to the structure coordinates of Argonaute. This would be followed by manual model building using software such as QUANTA or SYBYL.

Useful programs to aid one of skill in the art in connecting the individual chemical groups or fragments include:

1. CAVEAT (Bartlett et al., 1989, 'CAVEAT: A Program to Facilitate the Structure-Derived Design of Biologically Active Molecules.' In Molecular Recognition in Chemical and Biological Problems', Special Pub., Royal Chem. Soc. 78:182-196). CAVEAT is available from the University of California, Berkeley, Calif.;

2. 3D Database systems such as MACCS-3D (MDL Information Systems, San Leandro, Calif.). This area is reviewed in Martin, 1992, J. Med. Chem. 35:2145-2154); and

3. HOOK (available from Molecular Simulations, Burlington, Mass.).

Instead of proceeding to build a modulator of Argonaute in a step-wise fashion one fragment or chemical group at a time, as described above, Argonaute-binding compounds or modulators may be designed as a whole or 'de novo' using either an empty binding site or the surface of a protein that participates in protein/protein interactions in a co-complex, or optionally including some portion(s) of a known modulator(s). These methods include:

1. LUDI (Bohm, 1992, J. Comp. Aid. Molec. Design 6:61-78). LUDI is available from Molecular Simulations, Inc., San Diego, Calif.;

2. LEGEND (Nishibata & Itai, 1991, Tetrahedron 47:8985). LEGEND is available from Molecular Simulations, Burlington, Mass.; and

3. LeapFrog (available from Tripos, Inc., St. Louis, Mo.).

Other molecular modeling techniques may also be employed in accordance with this invention. See, e.g., Cohen et al., 1990, J. Med. Chem. 33:883-894. See also, Navia & Murcko, 1992, Current Opinions in Structural Biology 2:202-210.

Once a compound has been designed or selected by the above methods, the efficiency with which that compound may bind to Argonaute may be tested and

optimized by computational evaluation. An effective modulator of Argonaute must preferably demonstrate a relatively small difference in energy between its bound and free states (i.e., it must have a small deformation energy of binding). Thus, the most efficient modulators should preferably be designed with a deformation energy of binding of not greater than about 10 kcal/mol, preferably, not greater than 7 kcal/mol. Modulators may interact with the protein in more than one conformation that is similar in overall binding energy. In those cases, the deformation energy of binding is taken to be the difference between the energy of the free compound and the average energy of the conformations observed when the modulator binds to the protein.

A compound selected or designed for binding to or inhibiting Argonaute may be further computationally optimized so that in its bound state it would preferably lack repulsive electrostatic interaction with the target protein. Such non-complementary electrostatic interactions include repulsive charge-charge, dipole-dipole and charge-dipole interactions. Specifically, the sum of all electrostatic interactions between the modulator and the protein when the modulator is bound to it preferably make a neutral or favorable contribution to the enthalpy of binding.

Specific computer software is available in the art to evaluate compound deformation energy and electrostatic interaction. Examples of programs designed for such uses include: Gaussian 92, revision C (Frisch, Gaussian, Inc., Pittsburgh, Pa. ©1992); AMBER, version 4.0 (Kollman, University of California at San Francisco, ©1994); QUANTA/CHARMM (Molecular Simulations, Inc., Burlington, Mass., ©1994); and Insight II/Discover (Biosym Technologies Inc., San Diego, Calif., ©1994). These programs may be implemented, for instance, using a computer workstation, as are well-known in the art. Other hardware systems and software packages will be known to those skilled in the art.

The computer-assisted methods for designing a modulator of Argonaute activity can be de novo or based on a candidate compound. An example of a computer-assisted method for designing an modulator of Argonaute activity de novo would thus involve the steps of: (1) supplying a computer modeling application with a set of structure coordinates of a molecule or molecular complex comprising at least

a portion of an Argonaute; (2) computationally building a chemical entity represented by a set of structure coordinates; and (3) determining whether the chemical entity is an modulator expected to bind to or interfere with the molecule or molecular complex, wherein binding to or interfering with the molecule or molecular complex is indicative of potential modulation of Aargonaute activity.

Once an modulator or Argonaute binding compound has been optimally selected or designed, as described above, substitutions may then be made in some of its atoms or chemical groups in order to improve or modify its binding properties. Generally, initial substitutions are conservative, i.e., the replacement group will have approximately the same size, shape, hydrophobicity and charge as the original group. One of skill in the art will understand that substitutions known in the art to alter conformation should be avoided. Such altered chemical compounds may then be analyzed for efficiency of binding to Argonaute by the same computer methods described in detail above.

An example of such a computer-assisted method for identifying an modulator of Argonaute activity would thus involve (1) supplying a computer modeling application with a set of structure coordinates of a molecule or molecular complex comprising at least a portion of an Argonaute or Argonaute-like compound, (2) supplying the computer modeling application with a set of structure coordinates of a chemical entity; and (3) determining whether the chemical entity is an modulator expected to bind to or modulate the molecule or molecular complex.

The structure coordinates of an Argonaute co-complex, or of Argonaute alone, or of portions thereof, are particularly useful to solve the structure of other co-complexes of Argonaute, of mutants, of the Argonaute co-complex further complexed to another molecule, or of the crystalline form of any other protein or protein co-complex with significant amino acid sequence homology to any functional domain of Argonaute.

One method that may be employed for this purpose is molecular replacement. In this method, the unknown co-crystal structure, whether it is another Argonaute co-complex, a mutant, a Argonaute co-complex that is further complexed

to another molecule, or the crystal of some other protein or protein co-complex with significant amino acid sequence homology to any functional domain of one of the proteins in the co-complex crystal, may be determined using phase information from the present Argonaute co-complex structure coordinates. This method will provide an accurate three-dimensional structure for the unknown protein or protein co-complex in the new crystal more quickly and efficiently than attempting to determine such information ab initio.

If an unknown crystal form has the same space group as and similar cell dimensions to the known co-complex crystal form, then the phases derived from the known crystal form can be directly applied to the unknown crystal form, and in turn, an electron density map for the unknown crystal form can be calculated. Difference electron density maps can then be used to examine the differences between the unknown crystal form and the known crystal form. A difference electron density map is a subtraction of one electron density map, e.g., that derived from the known crystal form, from another electron density map, e.g., that derived from the unknown crystal form. Therefore, all similar features of the two electron density maps are eliminated in the subtraction and only the differences between the two structures remain. However, if the space groups and/or cell dimensions of the two crystal forms are different, then this approach will not work and molecular replacement must be used in order to derive phases for the unknown crystal form.

The techniques of X-ray diffraction can be employed in the study of the co-complexes of Argonaute. This information may thus be used to optimize known modulators of Argonaute and more importantly, to design and synthesize novel classes of modulators of Argonaute.

Subsets of the atomic structure coordinates can also be used in any of the above methods. Particularly useful subsets of the coordinates include, but are not limited to, coordinates of single domains, coordinates of residues lining an active site, coordinates of residues that participate in important protein-protein contacts at an interface, and Cα coordinates. For example, the coordinates of one domain of a protein that contains the active site may be used to design modulators that bind to that site, even though the protein is fully described by a larger set of atomic

coordinates. Therefore, as described in detail for the specific embodiments, below, a set of atomic coordinates that define the entire polypeptide chain, although useful for many applications, do not necessarily need to be used for the methods described herein.

II. Assay for Argonaute RNase Activity

The present application provides screening methods for agents that modulate the RNase activity of the Argonaute protein. Applicants have shown that Argonaute has a RNase H domain and acts as the Slicer enzyme of RISC to cleave mRNA bound by a single-stranded siRNA. Thus, the Argonaute activity can be assayed by measuring by any standard techniques in the art for measuring RNase activity. The exemplification provides one such example.

In certain embodiments, the RNase H activity of Argonaute can be measured. For example, WO 04/59012 describes a "Molecular Beacon" Assay for measuring RNase H activity and/or other nuclease-mediated cleavage of nucleic acids. Briefly, the assay detects degradation of a nucleic acid substrate which, preferably, is an RNA substrate that is annealed to at least one region or part of an oligonucleotide probe. In preferred embodiments, the oligonucleotide probe is a DNA probe (e.g., a deoxyoligonucleotide probe), which may also be referred to in the context of this invention as the DNA "substrate" moiety. Typically, both the oligonucleotide probe and the RNA substrate will be oligonucleotide molecules that are between about 10 and about 100 nucleotides in length and may be, e.g., between about 1050 nucleotides in length, more preferably between 15-25 nucleotides length. In preferred embodiments, the oligonucleotide probe is at least 18 nucleotides in length.

Chan et al. describes a capillary electrophoretic assay to measure RNase H activity. See Anal Biochem. 2004 Aug 15;331(2):296-302. Briefly, cleavage of a fluorescein-labeled RNA-DNA heteroduplex was monitored by capillary electrophoresis. This assay was used as a secondary assay to confirm hits from a high-throughput screening program. Since autofluorescent compounds in samples migrated differently from both substrate and product in most cases, the assay was

extremely robust for assaying enzymatic inhibition of such samples, in contrast to a simple well-based approach.

The screening methods may be conducted in a high-throughput fashion using any techniques available in the art. Recently, Parniak et al. described a fluorescence-based high-throughput screening assay for inhibitors of HIV RNase H activity. See Anal Biochem 2003, 322:33-9. Briefly, the assay substrate is an 18-nucleotide 3'-fluorescein-labeled RNA annealed to a complementary 18-nucleotide 5'-Dabcyl-modified DNA. The intact duplex has an extremely low background fluorescent signal and provides up to 50-fold fluorescent signal enhancement following hydrolysis. The size and sequence of the duplex are such that HIV-1 RT-RNase H cuts the RNA strand close to the 3' end. The fluorescein-labeled ribonucleotide fragment readily dissociates from the complementary DNA at room temperature with immediate generation of a fluorescent signal. This assay is rapid, inexpensive, and robust, providing Z' factors of 0.8 and coefficients of variation of about 5%. The assay can be carried out both in real-time (continuous) and in "quench" modes; the latter requires only two addition steps with no washing and is thus suitable for robotic operation. Several chemical libraries totaling more than 106,000 compounds were screened with this assay in approximately 1 month.

Alternatively, McLellan et al. described a nonradioactive, 96-well plate assay designed to be used for high-throughput screening of compounds capable of inhibiting the RNase H activity of HIV-1 reverse transcriptase. See McLellan at al., Biotechniques. 2002 Aug;33(2):424-9. In this method, tRNA is employed as substrate that was labeled with digoxygenin-modified reporter residues. The labeled tRNA was prehybridized with a DNA oligonucleotide that contained a single biotinylated residue at its 5'-terminus to ensure its attachment to streptavidin-coated microplates. The uncleaved, immobilized DNA/tRNA substrate was detected through the use of established ELISA protocols. Incubation with purified HIV-1 reverse transcriptase initiated RNase H degradation and caused a signal reduction to negligible background levels. In contrast, the signal intensity remained unaffected when using an RNase H deficient mutant enzyme. The assay was validated using

the hydrazone derivative BBNH that was previously shown to inhibit RNase H degradation below concentrations of 10 microM.

III. Reporter Gene Assay

The application also provides reporter gene assays. The reporter gene assays may be used to identify agents that modulate (e.g., increase) expression of Argonaute gene(s), e.g., by modulating Argonaute's promoter activity. For example, by operably linking an Argonaute's promoter with a reporter gene, the activity of the promoter can be monitored through monitoring/measuring the expression level of reporter gene. Many reporter gene assays have been developed and known to skilled artisans. Examples include: β-galactosidase assays; β-glucuronidase assays; B-lactamase assays (kits, β-lacatamase FRET substrates or color substrates are commercially available); CAT assays; Dual Reporter assays; GFP Assays; Luciferase Assays; SEAP Assays.

IV. Binding Assay

As described above, in silico screening or assays may be developed to identify a ligand or an inhibitor of interest, such as a ligand or an inhibitor that interacts with an Argonaute protein, e.g., a hAgo-2 protein. A ligand generally refers to a molecule (e.g., a nucleic acid molecule or a non-nucleic acid small molecule) that binds a molecule of interest (e.g., an Argonaute protein of the application). An inhibitor generally refers to a molecule that inhibits the function or activity of its target molecule, e.g., an Argonaute protein of the application.

A variety of assay formats will suffice and, in light of the present disclosure, those not expressly described herein will nevertheless be comprehended by one of ordinary skill in the art. Assay formats which approximate such conditions as formation of protein-based complexes and enzymatic activity may be generated in many different forms, and include assays based on cell-free systems, e.g., purified proteins or cell lysates, as well as cell-based assays which utilize intact cells. Simple binding assays can also be used to detect agents which bind to a protein of the application. Agents to be tested can be produced, for example, by bacteria, yeast

or other organisms (e.g., natural products), produced chemically (e.g., small molecules, including peptidomimetics), or produced recombinantly. In a preferred embodiment, the test agent is a small organic molecule, e.g., other than a peptide or oligonucleotide, having a molecular weight of less than about 6,000 daltons.

In many drug screening programs which test libraries of compounds and natural extracts, high throughput assays are desirable in order to maximize the number of compounds surveyed in a given period of time. Assays of the present application which are performed in cell-free systems, such as may be developed with purified or semi-purified proteins or with lysates, are often preferred as "primary" screens in that they can be generated to permit rapid development and relatively easy detection of an alteration in a molecular target which is mediated by a test compound. Moreover, the effects of cellular toxicity and/or bioavailability of the test compound can be generally ignored in the in vitro system, the assay instead being focused primarily on the effect of the drug on the molecular target as may be manifest in the affinity of the drug to the molecular target and/or changes in enzymatic properties of the molecular target.

In certain embodiments, an Argonaute protein to be used in a binding assay is at least semi-purified proteins. By semi-purified, it is meant that the proteins utilized in the reconstituted mixture have been previously separated from other cellular or viral proteins. For instance, in contrast to cell lysates, the protein involved in the protein-based complex formation are present in the mixture to at least 50% purity relative to all other proteins in the mixture, and more preferably are present at 90-95% purity.

Assaying the protein-based complexes of the application, in the presence or absence of a candidate agent, can be accomplished in any vessel suitable for containing the reactants. Examples include microtitre plates, test tubes, and micro-centrifuge tubes.

In an exemplary binding assay, the agent or compound of interest is contacted with an Argonaute protein. Detection and quantification of the Argonaute protein-based complex (e.g., a co-complex formed by the Argonaute protein and the

compound) provides a means for determining the compound's affinity for the Argonaute protein.

Protein-based complex formation may be detected by a variety of techniques, many of which are effectively described herein. For instance, formation of complexes can be quantitated using, for example, detectably labeled proteins (e.g., radiolabeled, fluorescently labeled, or enzymatically labeled), by immunoassay, or by chromatographic detection. Surface plasmon resonance systems, such as those available from Biacore International AB (Uppsala, Sweden), may also be used to detect binding interactions.

Often, it will be desirable to immobilize the protein to facilitate separation of complexes from uncomplexed forms of agents to be assayed for their binding affinity to a protein, as well as to accommodate automation of the assay. In an illustrative embodiment, a fusion protein can be provided which adds a domain that permits the protein (or a portion of the protein) to be bound to an insoluble matrix. For example, GST-Argonaute (or a portion thereof) fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined with test agents, e.g., a radio- or fluorescent-labeled agents, and incubated under conditions conducive to complex formation. Following incubation, the beads are washed to remove any unbound test agents, and the matrix bead-bound label(s) determined directly, or in the supernatant after the complexes are dissociated, e.g., when microtitre plate is used.

RNAi

The term "RNAi construct," as used herein, comprises nucleotides that hybridize under physiological condition to a portion of a target gene and attenuates expression of the target gene. In certain embodiments, the RNAi construct, when introduced into a cell, induces a sequence-specific RNA interference process. The RNAi construct used in the present application may be single-stranded siRNAs (ssRNAs), double-stranded siRNAs (dsRNAs), which includes short "hairpin" RNAs (shRNAs). An RNAi construct used in the present application may be single-stranded siRNAs (ssRNAs), double-stranded siRNAs (dsRNAs), which include

short "hairpin" RNAs (shRNAs). The RNAi construct may comprise one or more strands of polymerized ribonucleotide. It may include modifications to either the phosphate-sugar backbone or the nucleoside. For example, the phosphodiester linkages of natural RNA may be modified to include at least one of a nitrogen or sulfur heteroatom. Modifications in RNA structure may be tailored to allow specific genetic inhibition while avoiding a general panic response in some organisms which is generated by RNAi. Likewise, bases may be modified to block the activity of adenosine deaminase. The RNAi construct may be produced enzymatically or by partial/total organic synthesis, any modified ribonucleotide can be introduced by in vitro enzymatic or organic synthesis.

The RNAi construct may be directly introduced into the cell (i.e., intracellularly); or introduced extracellularly into a cavity, interstitial space, into the circulation of an organism, introduced orally, or may be introduced by bathing an organism in a solution containing RNA. Methods for oral introduction include direct mixing of RNA with food of the organism, as well as engineered approaches in which a species that is used as food is engineered to express an RNA, then fed to the organism to be affected. Physical methods of introducing nucleic acids include injection of an RNA solution directly into the cell or extracellular injection into the organism.

The double-stranded structure may be formed by a single self-complementary RNA strand (shRNA) or two complementary RNA strands. RNA duplex formation may be initiated either inside or outside the cell. The RNA may be introduced in an amount which allows delivery of at least one copy per cell. Higher doses (e.g., at least 5, 10, 100, 500 or 1000 copies per cell) of double-stranded material may yield more effective inhibition; lower doses may also be useful for specific applications. Inhibition is sequence-specific in that nucleotide sequences corresponding to the duplex region of the RNA are targeted for genetic inhibition.

RNAi constructs containing a nucleotide sequences identical to a portion, of either coding or non-coding sequence, of the target gene are preferred for inhibition. RNA sequences with insertions, deletions, and single point mutations relative to the target sequence (ds RNA similar to the target gene) have also been found to be

effective for inhibition. Thus, sequence identity may be optimized by sequence comparison and alignment algorithms known in the art (see Gribskov and Devereux, Sequence Analysis Primer, Stockton Press, 1991, and references cited therein) and calculating the percent difference between the nucleotide sequences by, for example, the Smith-Waterman algorithm as implemented in the BESTFIT software program using default parameters (e.g., University of Wisconsin Genetic Computing Group). Greater than 90% sequence identity, or even 100% sequence identity, between the inhibitory RNA and the portion of the target gene is preferred. Alternatively, the duplex region of the RNA may be defined functionally as a nucleotide sequence that is capable of hybridizing with a portion of the target gene transcript (e.g., 400 mM NaCl, 40 mM PIPES pH 6.4, 1 mM EDTA, 50 °C. or 70 °C. hybridization for 12-16 hours; followed by washing). In certain preferred embodiments, the length of the RNAi is at least 20, 21 or 22 nucleotides in length, e.g., corresponding in size to RNA products produced by Dicer-dependent cleavage. In certain embodiments, the RNAi construct is at least 25, 50, 100, 200, 300 or 400 bases. In certain embodiments, the RNAi construct is 400-800 bases in length.

In certain embodiments, an shRNA construct is designed with about 29 bp helices. Further information on the optimization of shRNA constructs may be found, for example, in the following references: Paddison, et al.. Proc Natl Acad Sci U S A, 2002. 99(3): p. 1443-8; 13. Brummelkamp, et al. Science, 2002. 21: p. 21; Kawasaki, et al. Nucleic Acids Res, 2003. 31(2): p. 700-7; Lee et al. Nat Biotechnol, 2002. 20(5): p. 500-5; Miyagishi, et al. Nat Biotechnol, 2002. 20(5): p. 497-500; Paul., et al., Nat Biotechnol, 2002. 20(5): p. 505-8.

The RNAi construct may be synthesized either in vivo or in vitro. Endogenous RNA polymerase of the cell may mediate transcription in vivo, or cloned RNA polymerase can be used for transcription in vivo or in vitro. For transcription from a transgene in vivo or an expression construct, a regulatory region (e.g., promoter, enhancer, silencer, splice donor and acceptor, polyadenylation) may be used to transcribe the RNAi strand (or strands). Inhibition may be targeted by specific transcription in an organ, tissue, or cell type; stimulation of an environmental condition (e.g., infection, stress, temperature, chemical inducers);

and/or engineering transcription at a developmental stage or age. The RNA strands may or may not be polyadenylated; the RNA strands may or may not be capable of being translated into a polypeptide by a cell's translational apparatus. The RNAi construct may be chemically or enzymatically synthesized by manual or automated reactions. The RNAi construct may be synthesized by a cellular RNA polymerase or a bacteriophage RNA polymerase (e.g., T3, T7, SP6). The use and production of an expression construct are known in the art (see also WO 97/32016; U.S. Pat. Nos. 5,593,874, 5,698,425, 5,712,135, 5,789,214, and 5,804,693; and the references cited therein). If synthesized chemically or by in vitro enzymatic synthesis, the RNA may be purified prior to introduction into the cell. For example, RNA can be purified from a mixture by extraction with a solvent or resin, precipitation, electrophoresis, chromatography or a combination thereof. Alternatively, the RNAi construct may be used with no or a minimum of purification to avoid losses due to sample processing. The RNAi construct may be dried for storage or dissolved in an aqueous solution. The solution may contain buffers or salts to promote annealing, and/or stabilization of the duplex strands.

Physical methods of introducing nucleic acids include injection of a solution containing the RNAi construct, bombardment by particles covered by the RNAi construct, soaking the cell or organism in a solution of the RNA, or electroporation of cell membranes in the presence of the RNAi construct. A viral construct packaged into a viral particle would accomplish both efficient introduction of an expression construct into the cell and transcription of RNAi construct encoded by the expression construct. Other methods known in the art for introducing nucleic acids to cells may be used, such as lipid-mediated carrier transport, chemical mediated transport, such as calcium phosphate, and the like. Thus the RNAi construct may be introduced along with components that perform one or more of the following activities: enhance RNA uptake by the cell, promote annealing of the duplex strands, stabilize the annealed strands, or other-wise increase inhibition of the target gene.

"Inhibition of gene expression" refers to the absence or observable decrease in the level of protein and/or mRNA product from a target gene. "Specificity" refers

to the ability to inhibit the target gene without manifest effects on other genes of the cell. The consequences of inhibition can be confirmed by examination of the outward properties of the cell or organism (as presented below in the examples) or by biochemical techniques such as RNA solution hybridization, nuclease protection, Northern hybridization, reverse transcription, gene expression monitoring with a microarray, antibody binding, enzyme linked immunosorbent assay (ELISA), Western blotting, radioimmunoassay (RIA), other immunoassays, and fluorescence activated cell analysis (FACS). For RNA-mediated inhibition in a cell line or whole organism, gene expression is conveniently assayed by use of a reporter or drug resistance gene whose protein product is easily assayed. Such reporter genes include acetohydroxyacid synthase (AHAS), alkaline phosphatase (AP), beta galactosidase (LacZ), beta glucoronidase (GUS), chloramphenicol acetyltransferase (CAT), green fluorescent protein (GFP), horseradish peroxidase (HRP), luciferase (Luc), nopaline synthase (NOS), octopine synthase (OCS), and derivatives thereof. Multiple selectable markers are available that confer resistance to ampicillin, bleomycin, chloramphenicol, gentamycin, hygromycin, kanamycin, lincomycin, methotrexate, phosphinothricin, puromycin, and tetracyclin.

Depending on the assay, quantitation of the amount of gene expression allows one to determine a degree of inhibition which is greater than 10%, 33%, 50%, 90%, 95% or 99% as compared to a cell not treated according to the present application. As an example, the efficiency of inhibition may be determined by assessing the amount of gene product in the cell: mRNA may be detected with a hybridization probe having a nucleotide sequence outside the region used for the inhibitory double-stranded RNA, or translated polypeptide may be detected with an antibody raised against the polypeptide sequence of that region.

As disclosed herein, the present application is not limited to any type of target gene or nucleotide sequence. In some preferred embodiments, the target gene is an essential gene or a gene which is essential for cell viability. The following classes of possible target genes are listed for illustrative purposes: developmental genes (e.g., adhesion molecules, cyclin kinase inhibitors, Writ family members, Pax family members, Winged helix family members, Hox family members, cytokines,

lymphokines and their receptors, growth/differentiation factors and their receptors, neurotransmitters and their receptors); oncogenes (e.g., ABLI, BCLI, BCL2, BCL6, CBFA2, CBL, CSFIR, ERBA, ERBB, EBRB2, ETSI, ETS1, ETV6, FGR, FOS, FYN, HCR, HRAS, JUN, KRAS, LCK, LYN, MDM2, MLL, MYB, MYC, MYCLI, MYCN, NRAS, PIM 1, PML, RET, SRC, TALI, TCL3, and YES); tumor suppressor genes (e.g., APC, BRCA1, BRCA2, MADH4, MCC, NF 1, NF2, RB 1, P53, BIM, PUMA and WTI); and enzymes (e.g., ACC synthases and oxidases, ACP desaturases and hydroxylases, ADP-glucose pyrophorylases, ATPases, alcohol dehydrogenases, amylases, amyloglucosidases, catalases, cellulases, chalcone synthases, chitinases, cyclooxygenases, decarboxylases, dextrinases, DNA and RNA polymerases, galactosidases, glucanases, glucose oxidases, granule-bound starch synthases, GTPases, helicases, hemicellulases, integrases, inulinases, invertases, isomerases, kinases, lactases, lipases, lipoxygenases, lysozymes, nopaline synthases, octopine synthases, pectinesterases, peroxidases, phosphatases, phospholipases, phosphorylases, phytases, plant growth regulator synthases, polygalacturonases, proteinases and peptidases, pullanases, recombinases, reverse transcriptases, RUBISCOs, topoisomerases, and xylanases).

The application also provides variations of the methods described herein, wherein gene expression of more than one gene is achieved. This may be achieved for example, by expressing multiple shRNAs, or by designing an shRNA to inhibit the gene expression of two or more genes which share substantial nucleotide sequence identity in a short stretch, preferably at least 90% identity over a length of 20, 22, 25, 27, or 30 nucleotides.

The compositions of the present application may be used to enhance the therapeutic effectiveness of a RNAi therapeutics. Exemplary RNAi therapeutics includes double-stranded ribonucleic acids (dsRNAs) for inhibiting the expression of a K-ras oncogene in a cell for treating pancreatic cancer, described in US20040121348, double-stranded ribonucleic acids (dsRNAs) having nucleotide sequences substantially identical to at least a part of a 3'-untranslated region (3'-UTR) of a (+) strand RNA virus useful for treating hepatitis C infection, described in US20040091457, siRNAs that down-regulate expression of neurite growth

inhibitor receptor, prostaglandin D2 receptor, IkappaB kinase or protein kinase PKR genes, useful for treating cancer and inflammatory disease, described in U.S. Patent Application Publication No. 20030191077.

Furthermore, the crystal structure, the electronic representation, as well as other aspects of the application also relate to a method for identifying, designing, and/or optimizing an RNAi construct or RNAi therapeutic of the application. For example, based on the structure of the PAZ domain, particular the site that may interact with the 3' end of a nucleic acid (e.g., an RNA or a portion of an RNAi construct), the nucleic acid sequence or structure may be designed and/or optimize to increase or decrease the nucleic acid's interaction with the PAZ domain. Similarly, based on the PIWI domain as well as the interface between the PIWI domain and the PAZ domain, an RNAi construct or RNAi therapeutic may be designed and/or optimized. An optimized RNAi therapeutic may have an improved pharmacokinetic and/or pharmacodynamic profile.

References

1. R. Jorgensen, Trends Biotechnol 8, 340-4. (1990).
2. D. Baulcombe, Arch Virol Suppl 15, 189-201. (1999).
3. R.F. Ketting, T.H. Haverkamp, H.G. van Luenen, R.H. Plasterk, Cell 99, 133-41 (1999).
4. I.M. Hall et al., Science 297, 2232-7. (2002).
5. T. Volpe et al., Science 22, 22 (2002).
6. G.J. Hannon, Nature 418, 244-51. (2002).
7. P.J. Paddison et al., Nature 428, 427-31 (2004).
8. A.G. Fraser et al., Nature 408, 325-30. (2000).
9. M. Boutros et al., Science 303, 832-5 (2004).
10. K. Berns et al., Nature 428, 431-7 (2004).
11. A. Fire et al., Nature 391, 806-11. (1998).
12. S.M. Hammond, E. Bernstein, D. Beach, G. J. Hannon, Nature 404, 293-6 (2000).
13. P.D. Zamore, T. Tuschl, P. A. Sharp, D. P. Bartel, Cell 101, 25-33 (2000).
14. A.J. Hamilton, D. C. Baulcombe, Science 286, 950-2 (1999).

15. S.M. Elbashir, J. Martinez, A. Patkaniowska, W. Lendeckel, T. Tuschl, Embo J 20, 6877-88 (2001).

16. E. Bernstein, A.A. Caudy, S. M. Hammond, G.J. Hannon, Nature 409, 363-6. (2001).

17. S. M. Elbashir, W. Lendeckel, T. Tuschl, Genes Dev 15, 188-200 (2001).

18. A. Nykanen, B. Haley, P. D. Zamore, Cell 107, 309-21. (2001).

19. D.P. Bartel, Cell 116, 281-297 (2004).

20. Y. Lee et al., Nature 425, 415-9 (2003).

21. A.A. Caudy, M. Myers, G.J. Hannon, S. M. Hammond, Genes Dev 16, 2491-6 (2002).

22. G. Hutvagner, P.D. Zamore, Science 297, 2056-60 (2002).

23. Z. Mourelatos et al., Genes Dev 16, 720-8. (2002).

24. T. Tuschl, P.D. Zamore, R. Lehmann, D.P. Bartel, P. A. Sharp, Genes Dev 13, 3191-7 (1999).

25. D. S. Schwarz, G. Hutvagner, B. Haley, P. D. Zamore, Mol Cell 10, 537-48 (2002).

26. J. Martinez, A. Patkaniowska, H. Urlaub, R. Luhrmann, T. Tuschl, Cell 110, 563-74 (2002).

27. M. A. Carmell, Z. Xuan, M. Q. Zhang, G. J. Hannon, Genes Dev 16, 2733-42. (2002).

28. D. N. Cox et al., Genes Dev 12, 3715-27 (1998).

29. J. J. Song et al., Nat Struct Biol 10, 1026-1032 (2003).

30. K. S. Yan et al., Nature 426, 468-74 (2003).

31. A. Lingel, B. Simon, E. Izaurralde, M. Sattler, Nature 426, 465-9 (2003).

32. A. Lingel, B. Simon, E. Izaurralde, M. Sattler, Nat Struct Mol Biol 11, 576-7 (2004).

33. J. B. Ma, K. Ye, D. J. Patel, Nature 429, 318-22 (2004).

34. H. Zhang, F. A. Kolb, V. Brondani, E. Billy, W. Filipowicz, Embo J 21, 5875-85. (2002).

35. A. M. Friedman, T. O. Fischmann, T. A. Steitz, Science 268, 1721-7 (1995).

36. F. Dyda et al., Science 266, 1981-6 (1994).

37. J. Lubkowski et al., Biochemistry 38, 13512-22 (1999).

38. M. Ariyoshi et al., Cell 78, 1063-72 (1994).

39. P. Rice, K. Mizuuchi, Cell 82, 209-20 (1995).

40. D. R. Davies, I.Y. Goryshin, W.S. Reznikoff, I. Rayment, Science 289, 77-85 (2000).

41. L. Lai, H. Yokota, L.W. Hung, R. Kim, S.H. Kim, Structure Fold Des 8, 897-904 (2000).

42. K. Katayanagi, M. Okumura, K. Morikawa, Proteins 17, 337-46 (1993).

43. B. R. Chapados et al., J Mol Biol 307, 541-56 (2001).

44. W. Yang, T. A. Steitz, Structure 3, 131-4 (1995).

45. D.R. Davies, L. M. Braam, W. S. Reznikoff, I. Rayment, J Biol Chem 274, 11904-13 (1999).

46. S. Kanaya, M. Ikehara, Subcell Biochem 24, 377-422 (1995).

47. M. Haruki, Y. Tsunaka, M. Morikawa, S. Iwai, S. Kanaya, Biochemistry 39, 13939-44 (2000).

48. L.S. Beese, T.A. Steitz, Embo J 10, 25-33 (1991).

49. T.A. Steitz, J.A. Steitz, Proc Natl Acad Sci U S A 90, 6498-502 (1993).

50. J. F. Davies, 2nd, Z. Hostomska, Z. Hostomsky, S.R. Jordan, D.A. Matthews, Science 252, 88-95 (1991).

51. K. Klumpp et al., Nucleic Acids Res 31, 6852-9 (2003).

52. D.S. Schwarz, Y. Tomari, P. D. Zamore, Curr Biol 14, 787-91 (2004).

53. J. Martinez, T. Tuschl, Genes Dev 18, 975-80 (2004).

54. U. Wintersberger, Pharmacol Ther 48, 259-80 (1990).

55. H. Huang, R. Chopra, G.L. Verdine, S. C. Harrison, Science 282, 1669-75 (1998).

56. S.G. Sarafianos et al., Embo J 20, 1449-61 (2001).

57. M.L. Kopka, L. Lavelle, G.W. Han, H.L. Ng, R.E. Dickerson, J Mol Biol 334, 653-65 (2003).

58. Y. Tomari et al., Cell 116, 831-41 (2004).

59. J.W. Pham, J.L. Pellino, Y.S. Lee, R.W. Carthew, E. J. Sontheimer, Cell 117, 83-94 (2004).

60. R.M. Esnouf, J. Mol. Graphics 15, 132-134 (1997).

61. P.J. Kraulis, J. Appl. Cryst. 24, 946-950 (1991).

62. D.J. Bacon, W. F. Anderson, J. Molec. Graphics 6, 219-220 (1988).

63. E.A. Merritt, M.E.P. Murphy, Acta Cryst. D50, 869-873 (1994).

64. A. Nicholls, K.A. Sharp, B. Honig, Proteins - Structure, Function and Genetics 11, 281-296 (1991).

All references cited herein including the numbered references above and others throughout the application are incorporated by reference in their entirety.

EQUIVALENTS

While this invention has been particularly shown above and in the following examples and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the invention encompassed by the appended claims.

EXEMPLIFICATION

Example 1. DNA constructs and site-directed mutagenesis

cDNAs encoding full length human Ago1, Ago2, and Ago3 were generated by RT-PCR from RNAs extracted from 293T, HeLa or S2 cells. Plasmids expressing various Argonaute proteins were made by cloning the cDNAs into a pcDNA3-based myc-epitope tagging vector. Mutations were introduced by site-directed mutagenesis using the QuickChange Kit (Stratagene).

Example 2. Human Cell Culture and transfection

Human 293T cells were cultured in DMEM (10% FBS) in a 37 °C incubator with 5% CO2. Cell transfections were carried out using calcium-phosphate buffer or Mirus TransIT-LT1 transfection reagent. Luciferase GL3 siRNA duplex was purchased from Dharmacon. siRNA transfection was carried out by using Oligofectamine (Invitrogen). Procedures for immunoprecipitation and immunoblotting were described previously (Caudy et al, Genes. Dev. 16, 2491 (2002)). Lysis buffer contained 0.5% NP-40, 150mM NaCl, 2 mM $MgCl_2$, 2mM $CaCl_2$ and 20mM Tris-HCl pH 7.5. Protease inhibitor and DTT (final 2mM) were

added immediately before lysis. The antibody to the myc tag (9E10) was purchased from Neomarker. RNAs associated with the Ago immunocomplexes were isolated using phenol-chloroform/chloroform extraction and ethanol precipitation. RNAs were stained using SYBR Gold from Molecular Probes. Small RNA Northern blotting was carried out as described previously (Caudy et al., *supra*).

Example 3. mRNA Cleavage assays and in vitro reconstitution of RISC activity

Capped and uniformly radiolabeled Luciferase mRNA target was in vitro transcribed using the Riboprobe system from Promega and was purified using PAGE as described previously. The immunoaffinity purified Ago complexes were first resuspended in 10 µl buffer containing 100mM KCl, 2mM $MgCl_2$ and 10mM Tris pH7.5. For in vitro reconstitution of RISC activity, 4 µl of 1 µM in vitro phosphorylated (except where noted) single-stranded siRNA, duplexed siRNA or single-stranded DNA were added to the mix and incubated at 30 °C for 30 minutes. The final reaction was carried out in 20 µl which also contained 1mM ATP, 0.2 mM GTP, 8 units of RNAsin, 0.3 µg Creatine phosphokinase and 25 mM creatine phosphate. No-ATP reactions lacked ATP, GTP and the regeneration system. After a 2 hour incubation at 30 °C , RNAs were extracted using Trizol and chloroform and precipitated with isopropyl alcohol.

Example 4. Gene targeting and mice

Targeting construct was obtained by screening the lambda phage 3' HPRT library described in (Zheng et al., Nucleic Acids Res. 27, 2354 (1999)). The resultant targeting construct, containing exons 3-6 of mAgo2, was electroporated into mouse embryonic stem (ES) cells. Targeted clones were injected into C57BL/6 blastocysts to generate chimeras, which were crossed with C57BL/6 mice. Mouse genotyping was performed by Southern blot after digestion of genomic DNA with HindIII. The probe was amplified from genomic DNA using primer sequences 5'GACAATAGTGCAGAGACTTGC3' and 5'GGGCAGCCTGAGAATTGA3'. GenBank Accession Number for mouse Ago2 is AB081472. The Ago2 gene trap cell line RRE192 was obtained from Bay Genomics(Stryke et al., Nucleic Acids Res. 31, 278 (2003)).

Example 5. In situ hybridization

In situ hybridization was performed on whole-mount embryos essentially as described (Belo et al., Mech Dev. 68, 45 (1997)). Riboprobes for in situ hybridization were synthesized from T7-promoter containing PCR products corresponding to the 3' UTRs of Ago2 or Ago3. The Ago2 probe was amplified from genomic DNA using the primers 5'AGCTGTGAAGGCTCTGAG3' and 5'CAGTCCTACAGGACAAATCT3', and the Ago3 probe was similarly constructed using primers, AGGCTGTACAGATTCACCAAGATA and CCTTTACAAGAATAGATGCACATT.

Example 6. MEF Culture, transfection, and gene silencing assays

Day 10.5 embryos were dissected and diced in trypsin. Mouse embryo fibroblasts (MEFs) were cultured in DMEM + 10% FBS. MEFs were transfected in 24 well plates using Lipofectamine reagent according to the manufacturer's recommendations. Where indicated, each well received 2.5 picomoles of siRNA and 1ug of plasmid DNA. Dual luciferase assays (Promega) were carried out by cotransfecting cells with plasmids containing firefly luciferase under the control of the SV40 promoter (pGL3-Control, Promega) and Renilla luciferase under the control of the SV40 early enhancer/promoter region (pSV40, Promega). Luciferase siRNA was obtained from Dharmacon (siStarter, anti-luc siRNA-1). GFP (pEGFP-C1) and dsRed (pDsRed-express-N1) plasmids were obtained from Clontech. EGFP siRNA was obtained from Dharmacon (EGFP duplex). Ago1 and Ago2 expression plasmids were as described for the IP experiments, except that proteins were fused to an HA tag rather than a myc tag. Constructs for the translational repression assay were kindly provided by P. Sharp (Doench et al., Genes Dev. 17, 438 (2003)).

Example 7. RT-PCRs

RNA was extracted from cells and embryos using Trizol Reagent. Reverse transcription was conducted using Superscript-II RT from Invitrogen according to manufacturer's instructions. Subsequent PCR reactions were carried out using the following primers (5'-3'): mAgo1, GCATTTCAAGCAGAAATATAACCTTCA

and AGACTTTGATCTCAATCCC
ATTGTAG. MAgo2, GTACTTCAAGGACAGGCACAAGCTG and
TGGCAATTGC
TTTGTTCCTGC. MAgo3, GCTGCAGCTGAAGTACCCACA and
GTACTGGAGCATA
GGTGCTGGAAGTA. Mouse β-actin, CACTATTGGCAACGAGCGGT and
CTTCATGGT
GCTAGGAGCCA.

Example 8. MiRNA microarrays

RNA was recovered from immunoprecipitates with Trizol (Invitrogen) and conjugated with a Cy3 dinucleotide using T4 RNA ligase (NEB). Labeled RNA was hybridized to microarrays containing probes to 152 human mature microRNA sequences, washed, and scanned on a Genepix 400B array scanner. Log-ratios of Cy3/Cy5 values were global median center normalized for Ago-1, Ago-2, Ago-3 immunoprecipitates. For the control immunoprecipitate, data was normalized by a constant that was the average of the normalization constant for the Ago-1, Ago-2, Ago-3 datasets. Data was sorted in descending order for the Ago-2 dataset and a heat map generated using Treeview (Stanford University).

Example 9. miRNA Microarray Results.

Ago1-, Ago2- and Ago3-associated RNAs were hybridized to microarrays that report the expression status of 152 human microRNAs. Patterns of associated RNAs were identical within experimental error in each case (Fig. 9, Panel A). Additionally, each of the tagged Ago proteins associated similarly with a co-transfected siRNA (Fig. 9, Panel C). Previous studies have used tagged siRNAs to affinity purify Argonaute-containing RISC (Martinez et al., *supra*). These preparations, containing mixtures of at least two mammalian Argonautes, were capable of cleaving synthetic mRNAs that were complementary to the tagged siRNA. The ability of purified complexes containing individual Argonaute proteins to catalyze similar cleavages was examined. Surprisingly, irrespective of the siRNA sequence, only Ago2-containing RISC was able to catalyze cleavage (Fig. 9, Panel

B; Fig. 14). All three Ago proteins were similarly expressed and bound similar amounts of transfected siRNA (Fig. 1 Panels C and D).

These results demonstrated that mammalian Argonaute complexes are biochemically distinct, with only a single family member being competent for mRNA cleavage. To examine the possibility that Ago proteins might also be biologically specialized, the mouse Ago2 gene were disrupted by targeted insertional mutagenesis (Fig. 15; Fig. 10, Panel A) (Zheng et al., *supra*). Intercrosses of Ago2 heterozygous produced only wild-type and heterozygous offspring, strongly suggesting that disruption of Ago2 produced an embryonic-lethal phenotype. Ago2 deficient mice display several developmental abnormalities beginning approximately halfway through gestation. Both gene-trap and in situ hybridization data of day 9.5 embryos show broad expression of Ago2 in the embryo, with some hotspots of expression in the forebrain, heart, limb buds and branchial arches (Fig 10, Panels F and G). The most prominent phenotype is a defect in neural tube closure (Fig. 10, Panels D and E), often accompanied by apparent mispatterning of anterior structures including the forebrain (Fig. 10, Panels C and D). Roughly half of the embryos display complete failure of neural tube closure in the head region (Fig. 10, Panel E), while all embryos display a wavy neural tube in more caudal regions. Mutant embryos also suffer from apparent cardiac failure. The hearts are enlarged, and often accompanied by pronounced swelling of the pericardial cavity (Fig. 10, Panel C). By day 10.5, mutant embryos are severely developmentally delayed compared to wildtype and heterozygous littermates (Fig. 10, Panel B). This large difference in size, like the apparent cardiac failure, may be accounted for by a general nutritional deficiency caused by yolk sac and placental defects (Conway et al., Genesis 35, 1 (2003)), as histological analysis reveals abnormalities in these tissues.

Not all Argonaute proteins are required for successful mammalian development (Deng et al., Cell 2, 819, (2002); Kuramochi-Miyagawa et al., Development 131, 839 (2004)). Ago subfamily members are expressed in overlapping patterns in humans (Sasaki et al., Genomics 82, 323 (2003)). In situ hybridization demonstrates overlapping expression patterns for Ago2 and Ago3 in mouse embryos (Fig 10, Panel F; Fig. 16). Considered together with the essentially

identical patterns of miRNA binding, the results suggest the possibility that the ability of Ago2 to assemble into catalytically active complexes might be critical for mouse development. Although most miRNAs regulate gene expression at the level of protein synthesis, recently miR196 has been demonstrated to cleave the mRNA encoding HoxB8, a developmental regulator (Yekta et al., Science 304, 594 (2004)). Evolutionary conservation of an essential cleavage-competent RISC in organisms in which miRNAs predominantly act by translational regulation raises the possibility that target cleavage by mammalian miRNAs might be more important and widespread than previously appreciated.

Numerous studies have indicated that experimentally triggered RNAi in mammalian cells proceeds through siRNA-directed mRNA cleavage since in many, but not all, cases reiterated binding sites are necessary for repression at the level of protein synthesis (see for example (Bartel, Cell 116, 281 (2004); Doench et al., *supra*; Kiriakidou et al., Genes Dev. 18, 1165 (2004)). If Ago2 were uniquely capable of assembling into cleavage competent complexes in mice, then embryos or cells lacking Ago2 might be resistant to experimental RNAi. To address this question, mouse embryo fibroblasts (MEF) were prepared from E10.5 embryos from Ago2 heterozygous intercrosses. RT-PCR analysis and genotyping revealed that wild-type, mutant and heterozygous MEF populations were obtained. Importantly, MEF also express other Ago proteins, including Ago1 and Ago3 (Fig. 11, Panel A). Ago2 null MEF were unable to repress gene expression in response to an siRNA (Fig. 11, Panel B; Fig. 17). This defect could be rescued by addition of a third plasmid that encoded human Ago2 but not by Ago1 (Fig. 11, Panel B). In contrast, responses were intact for a reporter of repression at the level of protein synthesis, mediated by an siRNA binding to multiple mismatched sites (Doench et al., *supra*) (Fig. 11, Panel C).

Example 10. Mapping of determinants for cleavage

Since Ago2 was unique in its ability form cleavage-competent complexes, determinants of this capacity were mapped. Deletion analysis indicated that an intact Ago2 was required for RISC activity (Fig. 18). Therefore, the sequence of highly conserved but cleavage-incompetent Ago proteins was used as a guide to the

construction of Ago2 mutants. A series of point mutations included H634P, H634A, Q633R, Q633A, H682Y, L140W, F704Y and T744Y. While all of these mutations retain siRNA binding activity and most retain cleavage activity, changes at Q633 and H634 have a profound effect on target cleavage (Fig. 12). Both the Q633R and H634P mutations, in which residues were changed to corresponding residues in Ago1/3, abolished catalysis. Changing H634 to A also inactivated Ago2, while a similar change, Q633A, was permissive for cleavage. Thus, even relatively conservative changes can negate the ability of Ago2 to form cleavage-competent RISC.

Several possibilities could explain a lack of cleavage activity for Ago2 mutants. Such mutations could interfere with the proper folding of Ago2. However, this seems unlikely as those same residues presumably permit proper folding in closely related Argonaute proteins, and mutant Ago2 proteins retained the ability to interact with siRNAs. Alternatively, cleavage-incompetent Ago2 mutants could lose the ability to interact with the putative Slicer. Finally, Ago2 itself might be Slicer, with the conservative substitutions altering the active center of the enzyme in a way that prevents cleavage. The last possibility predicted that an active enzyme with relatively pure Ago2 protein may be reconstituted. Ago2 was immunoaffinity purified from 293T cells and attempted to reconstitute RISC in vitro. Incubation with the double-stranded siRNA produced no significant activity, whereas Ago2 could be successfully programmed with single-stranded siRNAs to cleave a complementary substrate (Fig. 13, Panel A). Formation of the active enzyme was unaffected by first washing the immunoprecipitates with up to 2.5M NaCl or 1M urea. A 21nt single stranded DNA was unable to direct cleavage (Fig. 13, Panel A). Programming could be accomplished with different siRNAs that direct activity against different substrates (Fig. 19). RISC is formed though a concerted assembly process in which the RISC-Loading Complex (RLC) acts in an ATP-dependent manner to place one strand of the small RNA into RISC (Nykanen et al., Cell 107, 309 (2001); Pham et al., Cell 117, 83 (2004); Tomari et al., Cell 116, 831 (2004)). In vitro reconstitution occurs in the absence of ATP, suggesting that Ago2 could be programmed with siRNAs without a need for the normal assembly process (Fig. 13, Panel A). However, in vitro reconstitution of RISC still required the essential

characteristics of an siRNA. For example, single-stranded siRNAs that lack a 5' phosphate group cannot reconstitute an active enzyme.

While consistent with the possibility that the catalytic activity of RISC is carried within Ago2, these results do not rule out the possibility that a putative Slicer co-purifies with Ago2. To demonstrate more conclusively that Ago2 is Slicer, the crystal structure of an Argonaute protein from an archebacterium, *Pyrococcus furiosus*, was analyzed. This structure revealed that the PIWI domain folds into a structure analogous to the catalytic domain of RNAseH and ASV integrase. The notion that such a domain would lie at the center of RISC cleavage is consistent with previous observations. RNAseH and integrases cleave their substrates leaving 5' phosphate and 3' hydroxyl groups through a metal catalyzed cleavage reaction (Chapados et al., J. Mol. Biol. 307, 541 (2001); Yang et al., Strcuture 3, 131 (1995)). Notably, previous studies have strongly indicated that the scissile phosphate in the targeted mRNA is cleaved via a metal ion in RISC to give the same phosphate polarity (Schwarz et al., Curr. Biol. 14, 787 (2004)). The in vitro data are consistent with the reconstituted RISC also requiring a divalent metal (Fig. 20). The active center of RNAseH and its relatives consists of a catalytic triad of three carboxylate groups contributed by aspartic or glutamic acid (Chapados et al., *supra*; Yang et al., *supra*). These coordinate the essential metal and activate water molecules for nucleolytic attack. Reference to the known structure of RNAseH reveals two aspartate residues in the archeal Ago protein present at the precise spatial locations predicted for formation of an RNAseH-like active site. These align with identical residues in the human Ago2 protein (Fig. 21). Therefore, to test whether the PIWI domain of Ago2 provides catalytic activity to RISC, the two conserved aspartates, D597 and D669, were changed to alanine, with the prediction that either mutation would inactivate RISC cleavage. Consistent with this hypothesis, the mutant Ago2 proteins were incapable of assembling into a cleavage-competent RISC in vitro or in vivo, despite retaining the ability to bind siRNAs (Fig. 13, Panels B-D).

Considered together, the data provide strong support for the notion that Argonaute proteins are the catalytic components of RISC. Firstly, the ability to form an active enzyme is restricted to a single mammalian family member, Ago2. This

conclusion is supported both by biochemical analysis and by genetic studies in mutant MEF. Secondly, single amino acid substitutions within Ago2 that convert residues to those present in closely related proteins negate RISC cleavage. Thirdly, the structure of the P. furiosis Argonaute protein reveals provocative structural similarities between the PIWI domain and RNAseH domains, providing a hypothesis for the method by which Argonaute cleaves its substrates. This hypothesis was tested by introducing mutations in the predicted Ago2 active site.

Example 11. Protein expression and purification

The full length Argonaute gene from *Pyroccocus furiosus* (PfAgo) was cloned into a pSMT3 vector. PfAgo was expressed as an Smt3 fusion with an N-terminal histidine tag in BL21-RIPL cells. Smt3_Argonaute protein was purified with an NTA-agarose affinity column, and Smt3 was removed using Ulp1 protease, which cuts right after Smt3. The pSMT3 vector-Ulp1 protease system was a generous gift from Dr. Chris Lima. PfAgo was further purified with a heating step, as this protein is from a hyperthermophilic organism, anion exchange chromatography and gel filtration. Purified protein was concentrated to 12.5 mg/ml in 50mM Tris-HCl (pH8.0) and 300 mM NaCl. Se-Met substituted protein was expressed using metabolic inhibition of methionine biosynthesis as described in (G.D. Van Duyne, R.F. Standaert, P.A. Karplus, S.L. Schreiber, J. Clardy, J Mol Biol 229, 105-24 (1993)). Se-Met incorporation was confirmed by mass spectrometry.

Example 12. Crystallization and data collection

Initial crystals were grown by vapor diffusion using the hanging-drop method in the presence of organic solvents. The quality of crystals was significantly improved by several rounds of microseeding. Selenomethionine (Se-Met) substituted protein crystals were obtained by microseeding with native crystals. Mercury-derivatized crystals were prepared by soaking native crystals in 1mM p-chloromercuriphenylsulfonic acid for 5 hours. For cryoprotection crystals were soaked for 1 min in crystallization solution containing increasing amounts of ethylenglycol (EG) in 5% steps to a final EG concentration of 40%(v/v). Crystals

diffracted to approximately 2 Å resolution. All data were collected to a resolution of 2.25Å under cryogenic conditions (100K) at beamline X25 at the National Synchrotron Light Source (NSLS) at Brookhaven National Laboratory. Data were processed with HKL2000 (http://www.hkl-xray.com) (Table 1 provided in Figure 23).

Crystallization condition for native crystal:

1) Well solution as Water; and 2) Mixing 2 μl of 12.5 mg/ml PfAgo protein with 1 μl of water and 0.3 ul of 7% 1-butanol

Crystallization condition for Se-crystal:

1) Well solution as Water; and 2) Mixing 2 μl of 12.5 mg/ml PfAgo protein with 0.3 μl of 7% 1-butanol.

Example 13. Structure determination

Phases were calculated from a three-wavelength anomalous dispersion (MAD) experiment at the selenium inflection, peak and high remote energies using a Se-Met substituted crystal at the peak energy for the mercury derivative. 17 selenium sites were located using SnB (C.M. Weeks, R. Miller, J. of Applied Crystallography 32, 120-124 (1999)) and a single Hg site was located by calculating an anomalous difference Fourier map using initial phases calculated from the selenium data. Data from all three wavelengths for the Se-Met derivative and one wavelength for the Hg derivative were used for heavy atom site refinement by the program SHARP (E. delaFortelle, G. Bricogne, Meth. Enzymol. 276, 472-494 (1997)), followed by solvent flattening. A partial model was built using the program wARP (A. Perrakis, R. Morris, V.S. Lamzin, Nature Structure Biol. 6, 458-463 (1999)). The program SIGMAA (C.C.C.P.N.4. (Acta Crystallogr. D50, 760, Daresbury, UK, 1994)) was used to combine the partial structure model with the experimental phases. Iterative model building using the program O (T.A. Jones, M. Kjeldgaard, Methods Enzymol. 277, 173-208 (1997)) and crystallographic refinement with the program CNS (A.T. Brünger et al., Acta Crystallogr. D54, 905-921 (1998)) lead to the final model that contains 5913 protein atoms, and 77 water

molecules (Table 1 provided in Figure 23). Several loops are disordered in the structure and were not included: L26-G38, I253-K256, E278-V281, L347-L354, and S414-K442.

Example 14. UV crosslinking

PfAgo or GST were incubated with a 21-mer 5'-32 P-labeled ssRNA with an IodoU at the 5' end and unlabeled competitor ssRNA for 30 min at 30 °C. Incubation was carried out in 10 mM Tris-HCl (pH 7.5), 2 mM $MgCl_2$, and 150 mM KCl. UV crosslinking was done using a Stratalinker (Stratagene) at 312 nm for 20 min at room temperature. Double-stranded RNA probes were gel purified after annealing the 5'- ^{32}P-labeled ssRNA with an unlabeled complementary strand to form a ds-siRNA (including a 2-nucleotide 3'overhang and a 5'-phosphate group).

CLAIMS

1. A crystalline Argonaute.

2. A method of determining the three-dimensional structure of an Argonaute protein or a mutant, derivative, variant, analogue, homologue, sub-domain or fragment thereof comprising:

(a) aligning the amino acid sequence of the Argonaute mutant, derivative, variant, analogue, homologue, sub-domain or fragment with the amino acid sequence set forth in SEQ ID NO: 5 to match homologous regions of the amino acid sequences;

(b) modelling the structure of the matched homologous regions of said target Argonaute protein of unknown structure on the corresponding regions of the Argonaute protein structure as defined by the atomic co-ordinates as set forth in Table 3; and

(c) determining a conformation for the Argonaute mutant, derivative, variant, analogue, homologue, sub-domain or fragment which substantially preserves the structure of said matched homologous regions.

3. A method of identifying an agent that binds an Argonaute protein comprising:

(a) applying a 3-dimensional molecular modeling algorithm to the atomic coordinates of an Argonaute protein shown in Table 3 to determine the spatial coordinates of the binding pocket of the Argonaute protein; and

(b) electronically screening the stored spatial coordinates of a set of candidate agents against the spatial coordinates of the Argonaute protein binding pocket to identify agents that can bind to the Argonaute protein.

4. A computer-based method for the analysis of the interaction of a molecular structure with an Argonaute protein, comprising:

(a) providing a structure comprising a three-dimensional representation of said Argonaute protein or a portion thereof, which representation comprises all or a portion of the coordinates set forth in Table 3;

(b) providing a molecular structure to be fitted to said Argonaute protein structure; and

(c) fitting the molecular structure to the Argonaute protein structure of (a).

5. A computer-readable storage medium encoded with the atomic coordinates or an Argonaute protein as shown in Table 3.

6. A data array comprising the atomic coordinates of an Argonaute protein as set forth in Table 3.

7. An electronic representation of a crystal structure of an Argonaute protein.

8. An electronic representation of a binding site of the Argonaute protein.

9. An electronic representation of a domain of the Argonaute protein.

10. An electronic representation of an agent in a binding site of an Argonaute protein.

11. A method for obtaining a crystal of an Argonaute protein, comprising subjecting an Argonaute protein at 10-15 mg/ml to crystallization conditions for a time sufficient for crystal formation.

12. A method of identifying an agent that modulates the activity of an RNAi construct, comprising identifying an agent that modulates the expression and/or activity of an Argonaute protein.

13. A method of identifying an agent that potentiates the activity of an RNAi construct, comprising identifying an agent that increases the expression and/or activity of an Argonaute protein.

14. A method of identifying an agent that modulates the activity of an RNAi construct comprising:

(a) providing an isolated or recombinant Argonaute protein; and

(b) assaying the activity of said Argonaute protein in the presence of a candidate agent,

wherein a change in the activity of said Argonaute protein in the presence of a candidate agent is indicative of said candidate agent capable of modulating the activity of an RNAi construct.

15. A composition for targeted gene inhibition comprising an agent that modulates the RNase activity of an Argonaute protein.

16. A pharmaceutical composition comprising the composition of claim 15 and a physiologically acceptable carrier.

17. A cell line that overexpresses an Argonaute protein.

18. An assay for identifying nucleic acid sequences for conferring a particular phenotype in a cell, comprising:

(a) constructing a library of nucleic acid sequences oriented to produce double stranded RNA;

(b) introducing a dsRNA library into a culture of target cell line of claim 17;

(c) identifying members of the library which confer a particular phenotype on the cell, and identifying the sequence from the cell which is identical or homologous to the library member.

19. A nucleic acid composition comprising:

(a) a first nucleic acid comprising an RNAi construct and

(b) a second nucleic acid encoding an Argonaute protein.

20. The nucleic acid composition of claim 19, wherein the RNAi construct comprises a nucleotide sequence encoding a single-strand siRNA.

21. A pharmaceutical composition comprising the nucleic acid composition of claim 19 and a physiologically acceptable carrier.

22. A cell expressing the nucleic acid composition of claim 19.

Fig 1

Fig 2A

Fig 2B

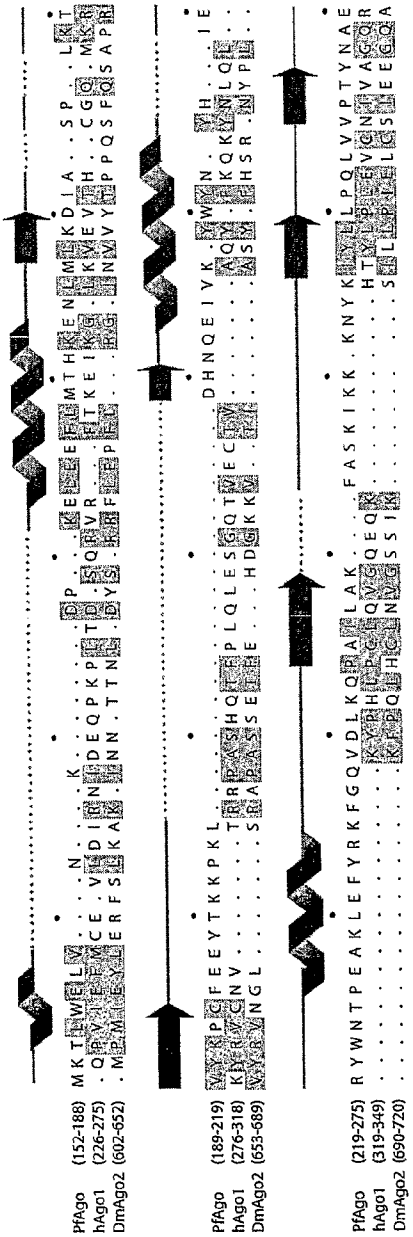

PfAgo (152-188)
hAgo1 (226-275)
DmAgo2 (602-652)
PfAgo (189-219)
hAgo1 (276-318)
DmAgo2 (653-689)
PfAgo (219-275)
hAgo1 (319-349)
DmAgo2 (690-720)

Fig 3A,B

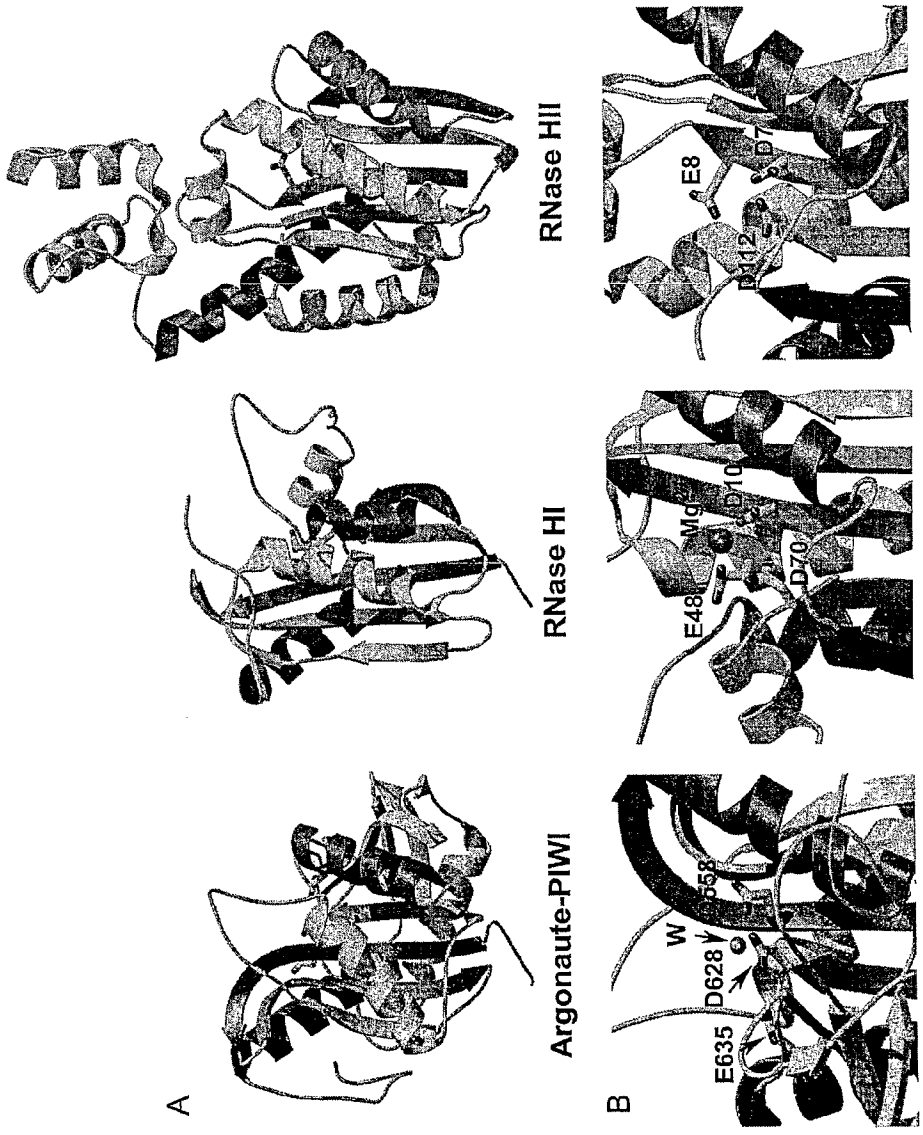

A
B
Argonaute-PIWI
RNase HI
RNase HII
E635
D628
W
558
E48
Mg
D10
D70
E8
D12
D7

Fig 3C

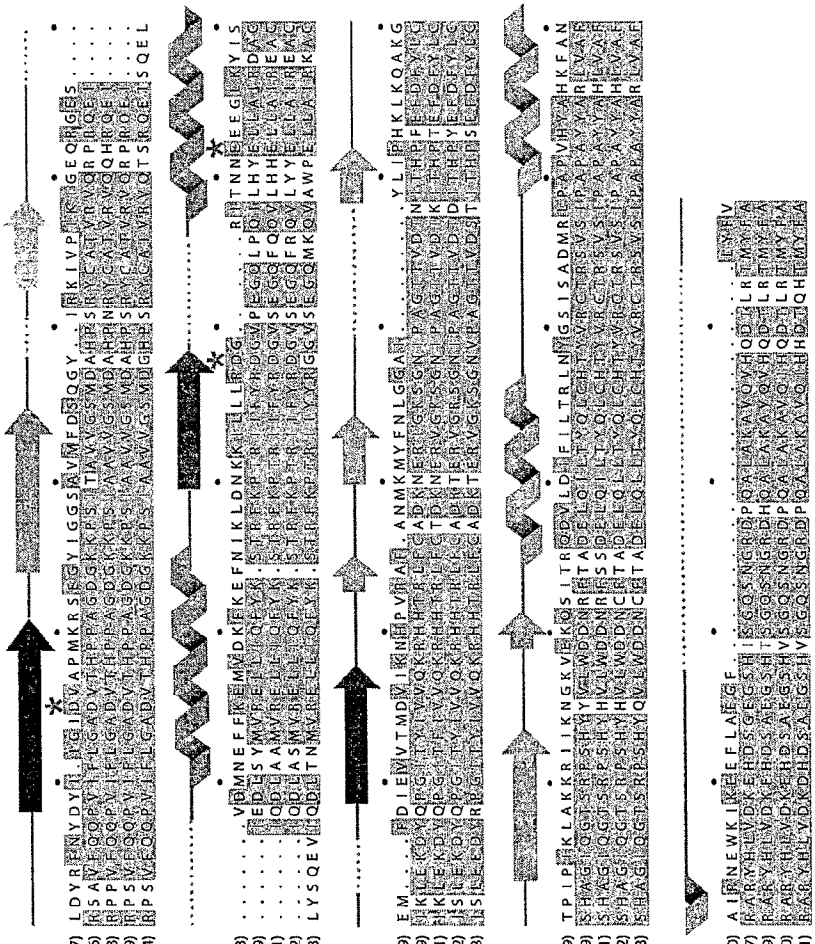


Fig 4

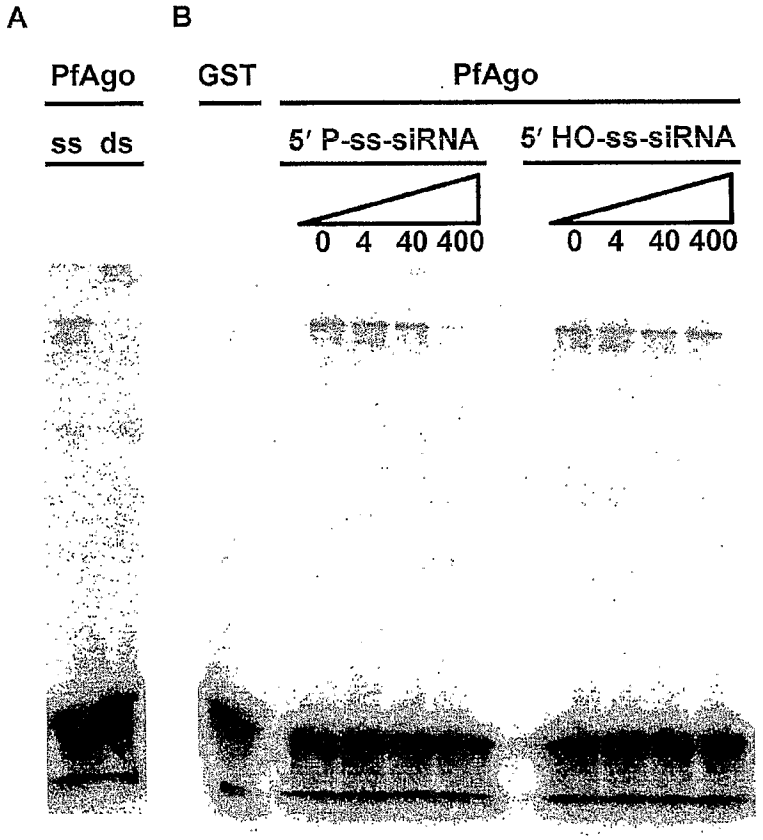

A
B
PfAgo
ss ds
GST
PfAgo
5′ P-ss-siRNA
5′ HO-ss-siRNA
0 4 40 400
0 4 40 400

Fig 5A

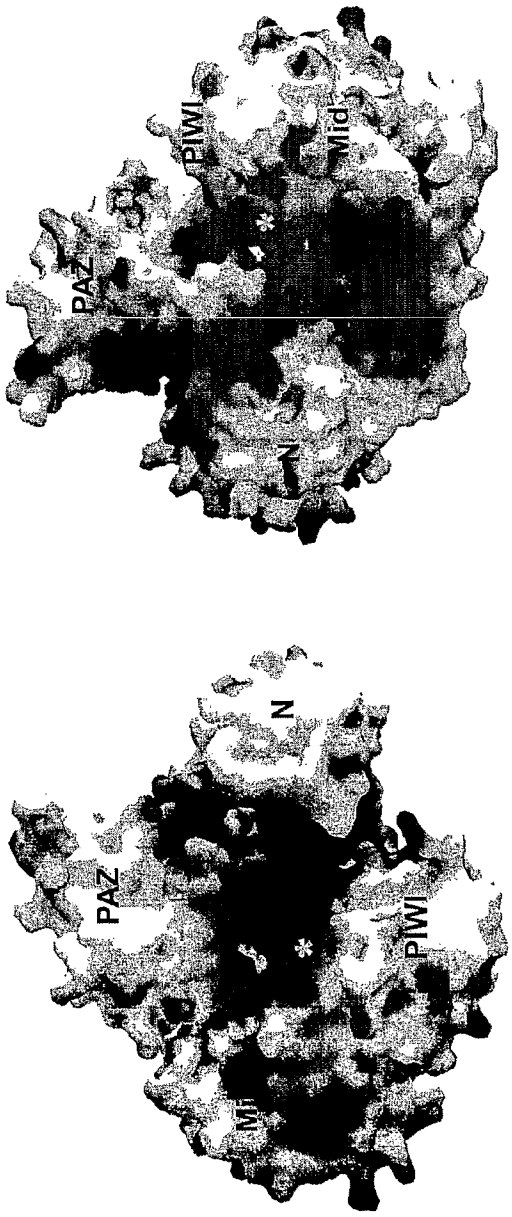


Fig 5B

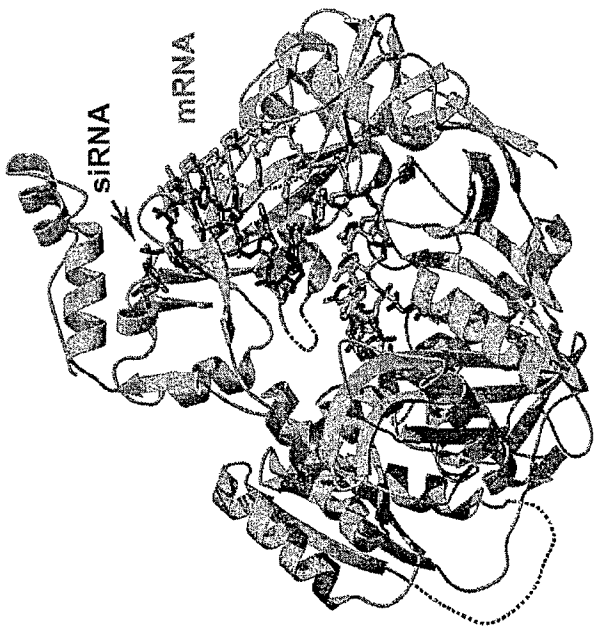
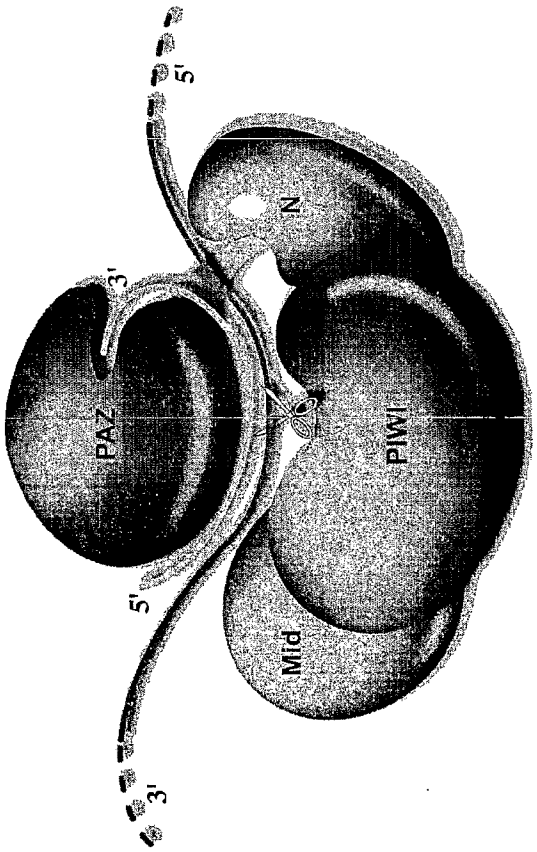


Fig 5C



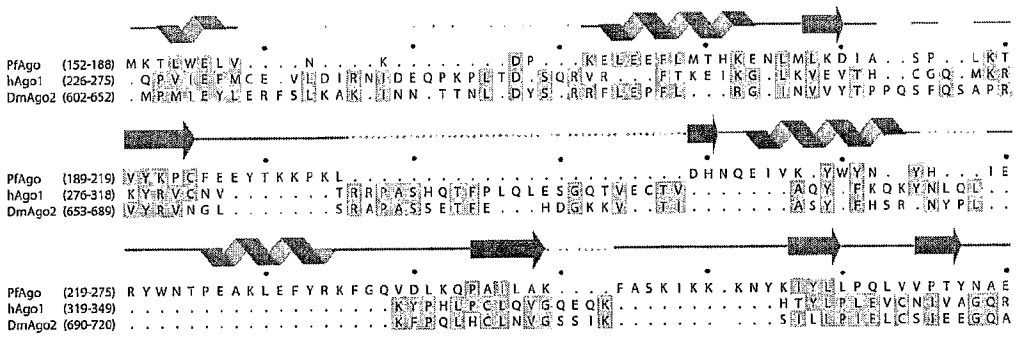

PfAgo (152-188) MKTLWELV....N....K.....DP...KELEEFLMTHKENLMLKDIA..SP..LKT
hAgo1 (226-275) .QPVLEFMCE.VLDIRNIDEQPKPLTD.SQRVR...FTKEIKG.LKVEVTH..CGQ.MKR
DmAgo2 (602-652) .MPMLEYLERFSLKAK.INN.TTNL.DYS.RRFLEPFL...RG.LNVVYTPPQSFQSAPR
PfAgo (189-219) VYKPCFEEYTKKPKL.....DHNQEIVK.YWYN..YH...IE
hAgo1 (276-318) KYRVCNV.....TRRPASHQTFPLQLESGQTVECTV.....AQY.FKQKYNLQL..
DmAgo2 (653-689) VYRVNGL.....SRADASSEITEE...HDGKKV..TI.....ASY.EHSR.NYPL..
PfAgo (219-275) RYWNTPEAKLEFYRKFGQVDLKQPALLAK....FASKIKK.KNYKIYLLPQLVVPTYNAE
hAgo1 (319-349) .....KYPHLPCLQVGQEQK.....HTVLPLEVCNLVAGQR
DmAgo2 (690-720) .....KFPQLHCLNVGSSIK.....SLLLPLELCSHEEGQA

Figure 6

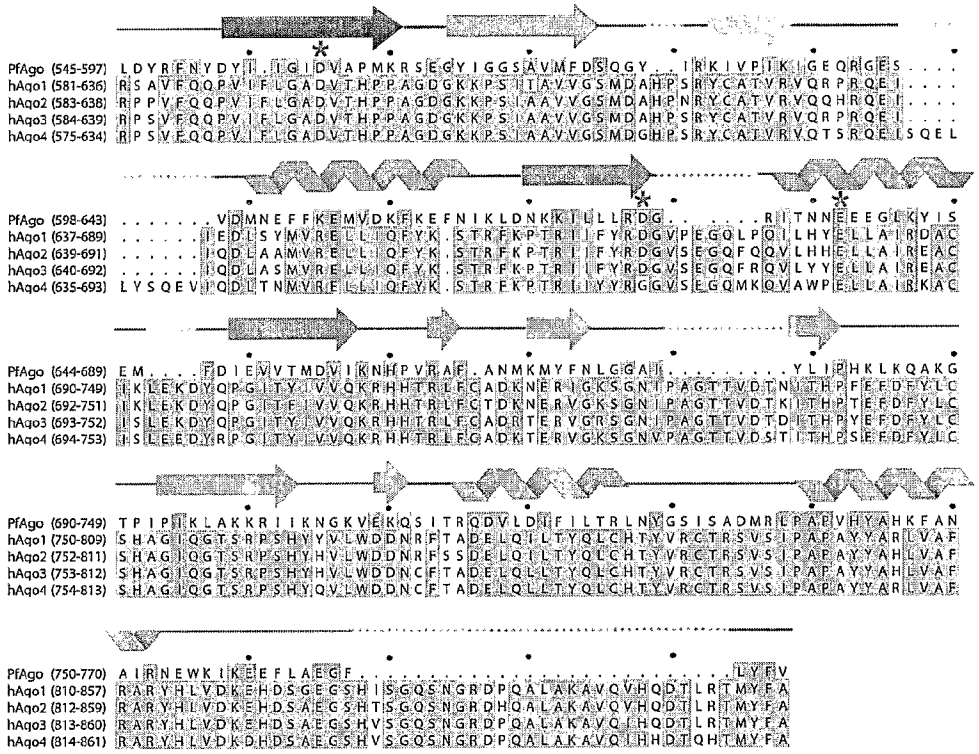

PfAgo (545-597) LDYRFNYDYTIGIDVAPMKRSEGYIGGSAVMFDSQGY..IRKIVPIKGEQRGES....
hAqo1 (581-636) RSAVFQQPVIFLGADVTHPPAGDGKKPSIAVVGSMDAHPSRYCATVRVQRPRQEI....
hAqo2 (583-638) RPPVFQQPVIFLGADVTHPPAGDGKKPSAAVVGSMDAHPNRYCATVRVQQHRQEI....
hAqo3 (584-639) RPSVFQQPVIFLGADVTHPPAGDGKKPSAAVVGSMDAHPSRYCATVRVQRPRQEI....
hAqo4 (575-634) RPSVFQQPVIFLGADVTHPPAGDGKKPSAAVVGSMDGHPSRYCATVRVQTSRQELSQEL
PfAgo (598-643) .....VDMNEFFKEMVDKFKEFNIKLDNKKILLLRDG.....RITNNEEGLKYIS
hAqo1 (637-689) .....IEDLSYMVRELLQFYK.STRFKPTRIIFYRDGVPEGQLPQILHYELLAIREAC
hAqo2 (639-691) .....IQDLAAMVRELLQFYK.STRFKPTRIIFYRDGVSEGQFQQVLHHELLAIREAC
hAqo3 (640-692) .....IQDLASMVRELLQFYK.STRFKPTRIIFYRDGVSEGQFRQVLYYELLAIREAC
hAqo4 (635-693) LYSQEVIQDLTNMVRELLQFYK.STRFKPTRIIYYRGGVSEGQMKQVAWPELLAIRKAC
PfAgo (644-689) EM....FDIEVVTMDVIKNHPVRAF.ANMKMYFNLGGAI.....YLIPHKLKQAKG
hAqo1 (690-749) IKLEKDYQPGITYVVQKRHHTRLFCADKNERIGKSGNIPAGTTVDTNITHPFEFDFYLC
hAqo2 (692-751) IKLEKDYQPGITFIVQKRHHTRLFCTDKNERVGKSGNIPAGTTVDTKITHPTEFDFYLC
hAqo3 (693-752) ISLEKDYQPGITYVVQKRHHTRLFCADRTERVGRSGNIPAGTTVDTDITHPYEFDFYLC
hAqo4 (694-753) ISLEEDYRPGITYVVQKRHHTRLFCADKTERVGKSGNVPAGTTVDSITTHPSEEDFYLC
PfAgo (690-749) TPIPIKLAKKRIIKNGKVEIKQSITRQDVLDIFILTRLNYGSISADMRLPAFVHYAHKFAN
hAqo1 (750-809) SHAGIQGTSRPSHYYVLWDDNRFTADELQILTYQLCHTYVRCTRSVSIPAPAYYARLVAF
hAqo2 (752-811) SHAGIQGTSRPSHYHVLWDDNRFSSDELQILTYQLCHTYVRCTRSVSIPAPAYYAHLVAF
hAqo3 (753-812) SHAGIQGTSRPSHYHVLWDDNCFTADELQLLTYQLCHTYVRCTRSVSIPAPAYYAHLVAF
hAqo4 (754-813) SHAGIQGTSRPSHYQVLWDDNCFTADELQLLTYQLCHTYVRCTRSVSIPAPAYYARLVAF
PfAgo (750-770) AIRNEWKIKEEFLAEGF.....LYFV
hAqo1 (810-857) RARYHLVDKEHDSGEGSHISGQSNGRDPQALAKAVQVHQDTLRTMYFA
hAqo2 (812-859) RARYHLVDKEHDSAEGSHTSGQSNGRDHQALAKAVQVHQDTLRTMYFA
hAqo3 (813-860) RARYHLVDKEHDSAEGSHVSGQSNGRDPQALAKAVQIHQDTLRTMYFA
hAqo4 (814-861) RARYHLVDKDHDSAEGSHVSGQSNGRDPQALAKAVQIHHDTQHTMYFA

Figure 7

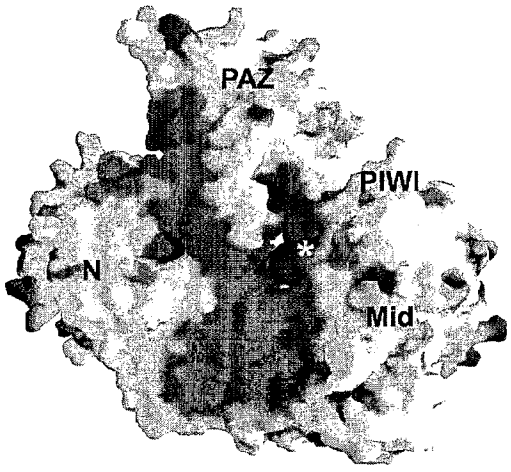


Figure 8

Figure 9

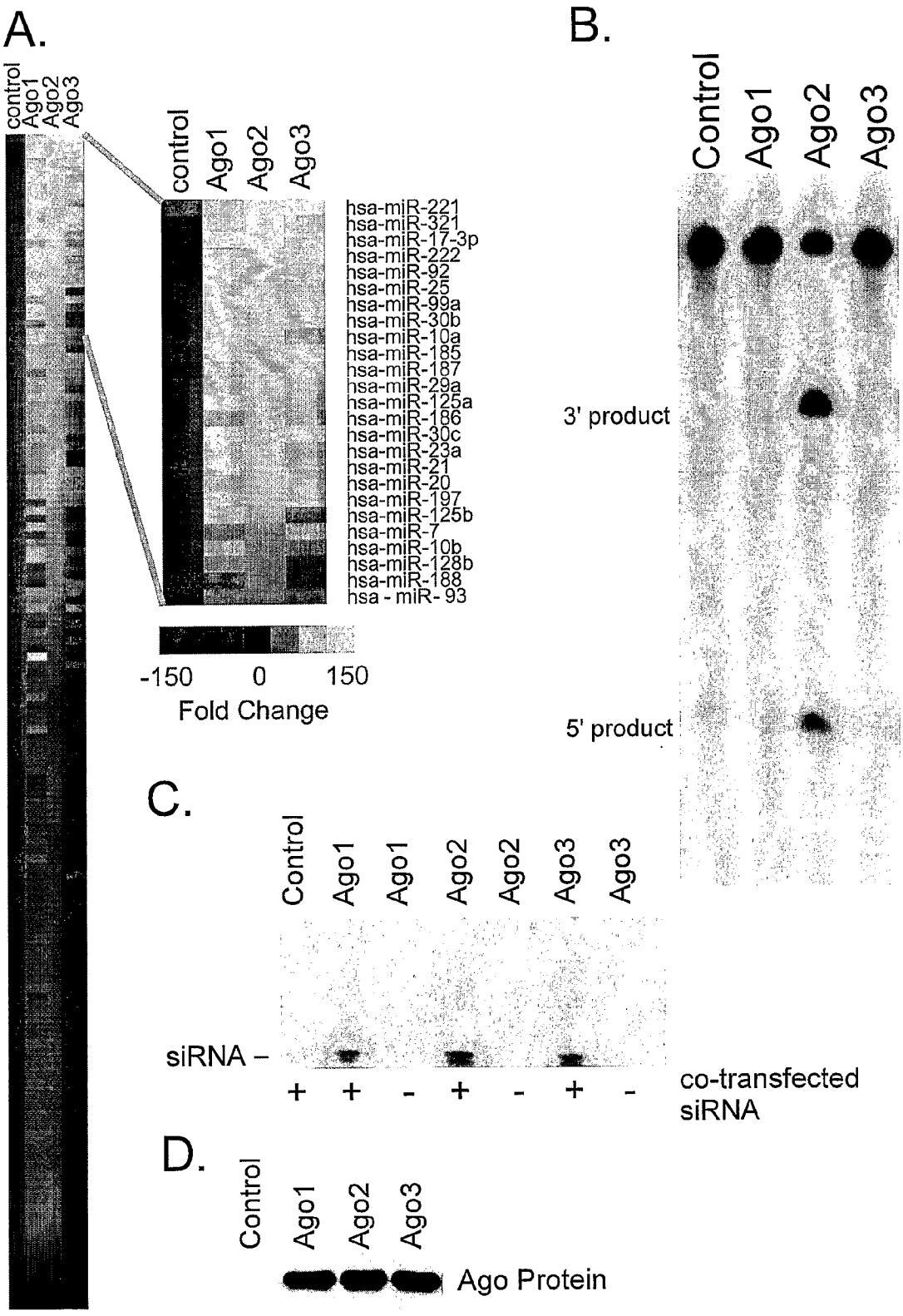

A.
control
Ago1
Ago2
Ago3
hsa-miR-221
hsa-miR-321
hsa-miR-17-3p
hsa-miR-222
hsa-miR-92
hsa-miR-25
hsa-miR-99a
hsa-miR-30b
hsa-miR-10a
hsa-miR-185
hsa-miR-187
hsa-miR-29a
hsa-miR-125a
hsa-miR-186
hsa-miR-30c
hsa-miR-23a
hsa-miR-21
hsa-miR-20
hsa-miR-197
hsa-miR-125b
hsa-miR-7
hsa-miR-10b
hsa-miR-128b
hsa-miR-188
hsa - miR- 93
-150
0
150
Fold Change
B.
Control
Ago1
Ago2
Ago3
3' product
5' product
C.
Control
Ago1
Ago1
Ago2
Ago2
Ago3
Ago3
siRNA –
+ + - + - + -
co-transfected siRNA
D.
Control
Ago1
Ago2
Ago3
Ago Protein

Figure 10

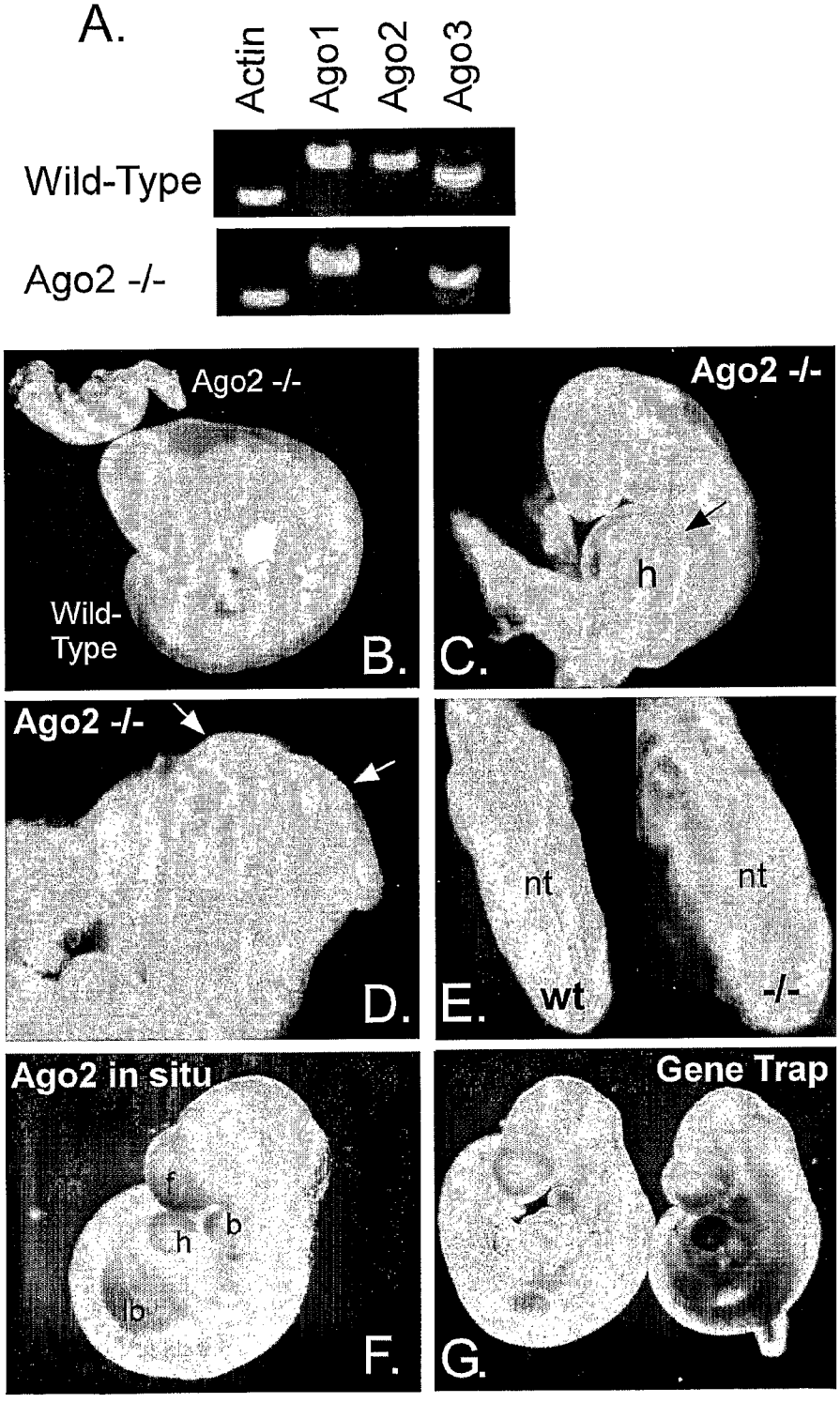
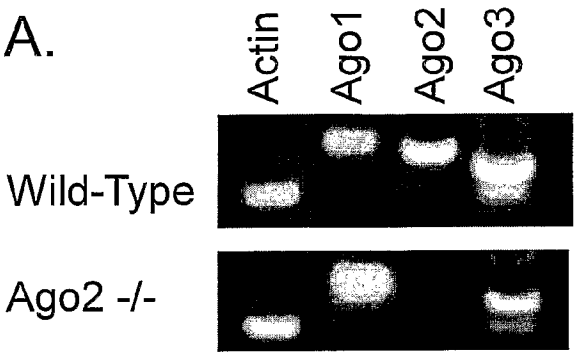
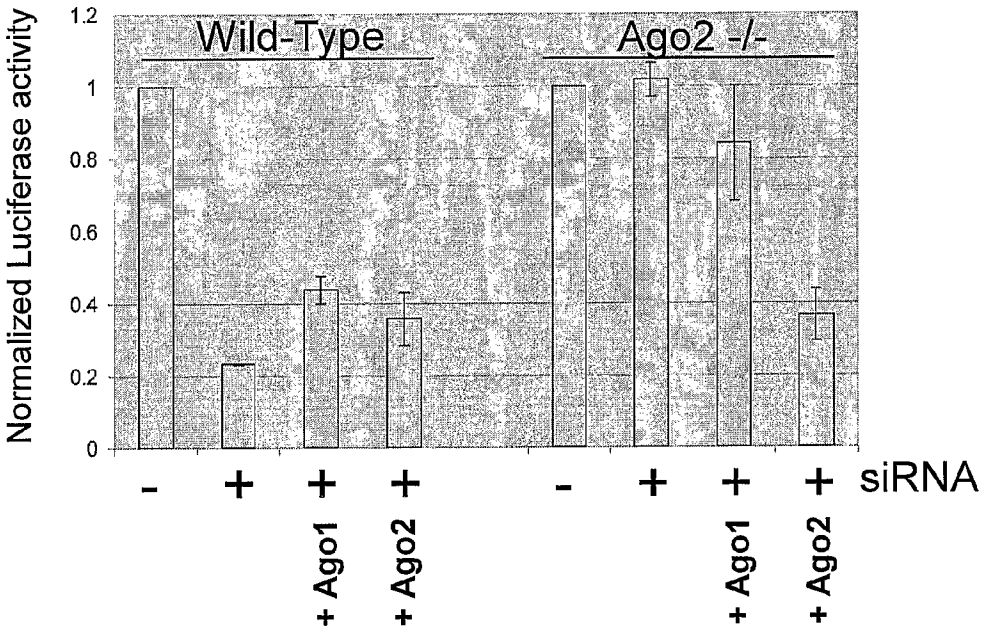

A.
Actin
Ago1
Ago2
Ago3
Wild-Type
Ago2 -/-
Ago2 -/-
Wild-Type
B.
Ago2 -/-
h
C.
Ago2 -/-
D.
nt
nt
wt
-/-
E.
Ago2 in situ
f
h
b
lb
F.
Gene Trap
G.

Figure 11

A.



B.



C.

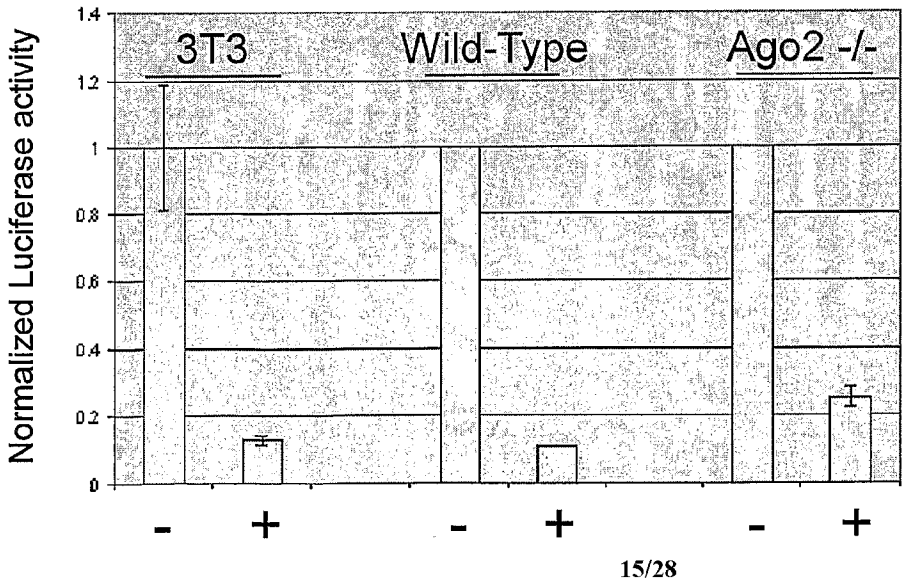
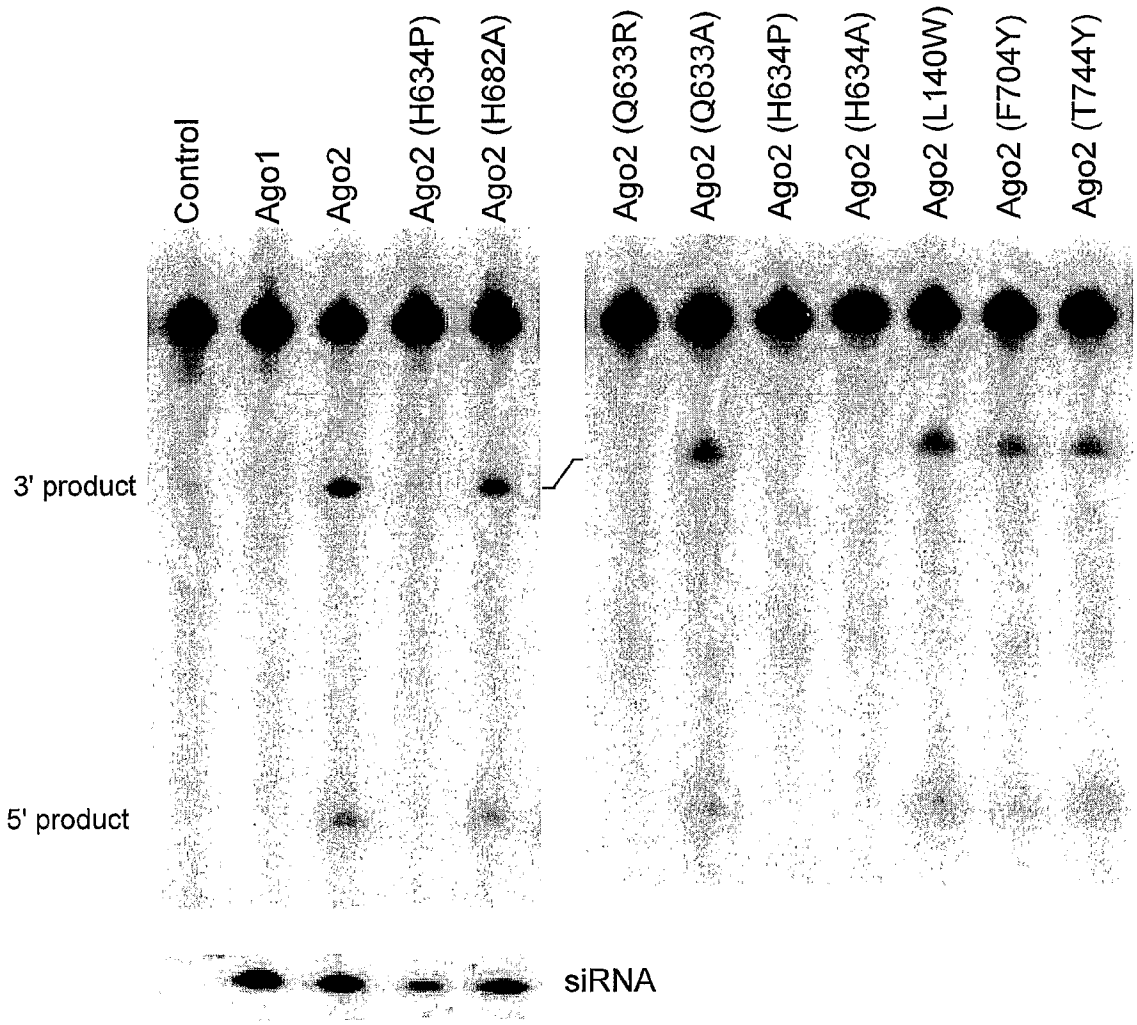
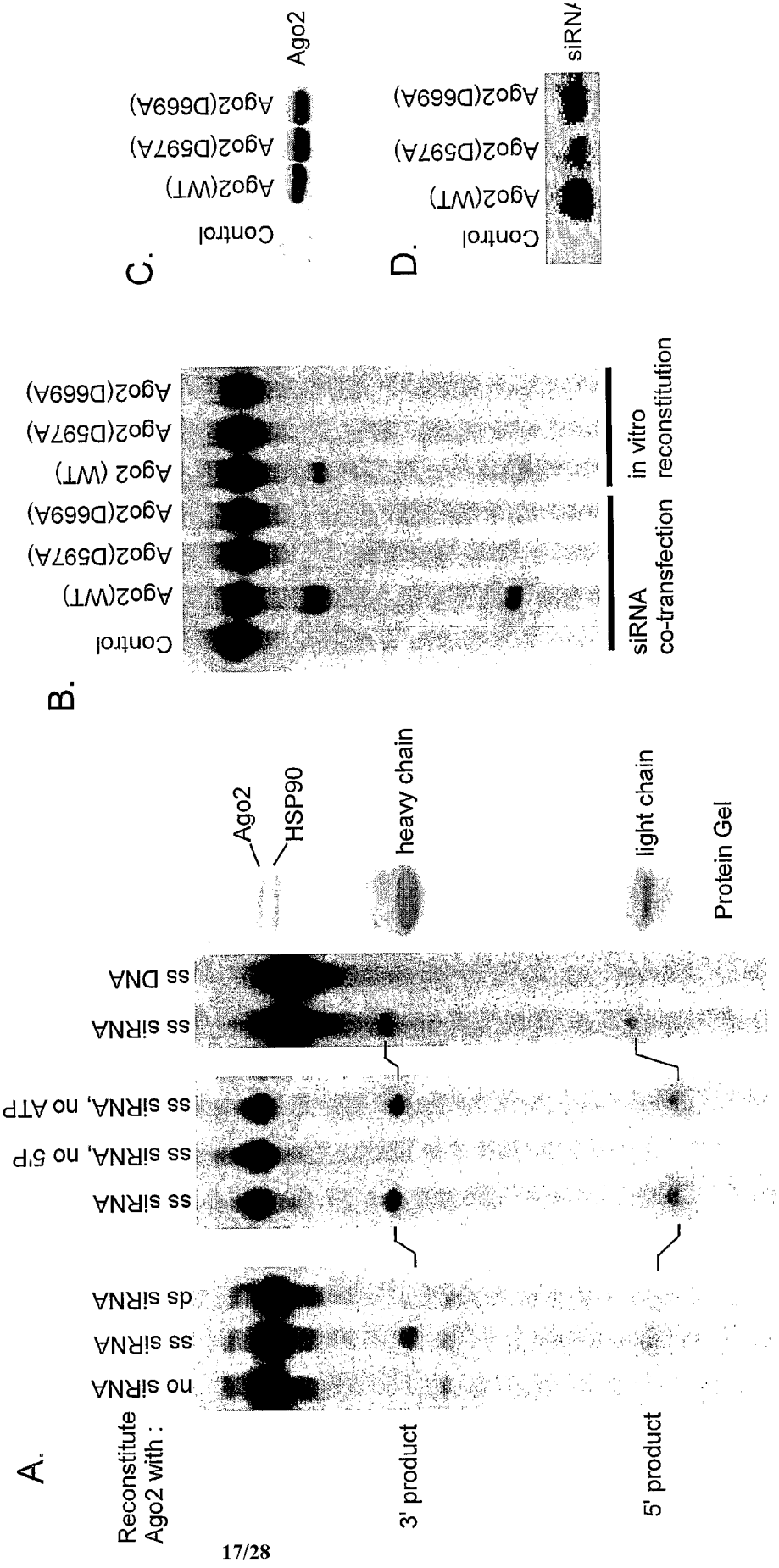


Figure 12


Control
Ago1
Ago2
Ago2 (H634P)
Ago2 (H682A)
Ago2 (Q633R)
Ago2 (Q633A)
Ago2 (H634P)
Ago2 (H634A)
Ago2 (L140W)
Ago2 (F704Y)
Ago2 (T744Y)
3' product
5' product
siRNA


A.
Reconstitute Ago2 with :
no siRNA
ss siRNA
ds siRNA
ss siRNA
ss siRNA, no 5'P
ss siRNA, no ATP
ss siRNA
ss DNA
3' product
5' product
Ago2
HSP90
heavy chain
light chain
Protein Gel
B.
Control
Ago2(WT)
Ago2(D597A)
Ago2(D669A)
Ago2 (WT)
Ago2(D597A)
Ago2(D669A)
siRNA co-transfection
in vitro reconstitution
C.
Control
Ago2(WT)
Ago2(D597A)
Ago2(D669A)
Ago2
D.
Control
Ago2(WT)
Ago2(D597A)
Ago2(D669A)
siRNA

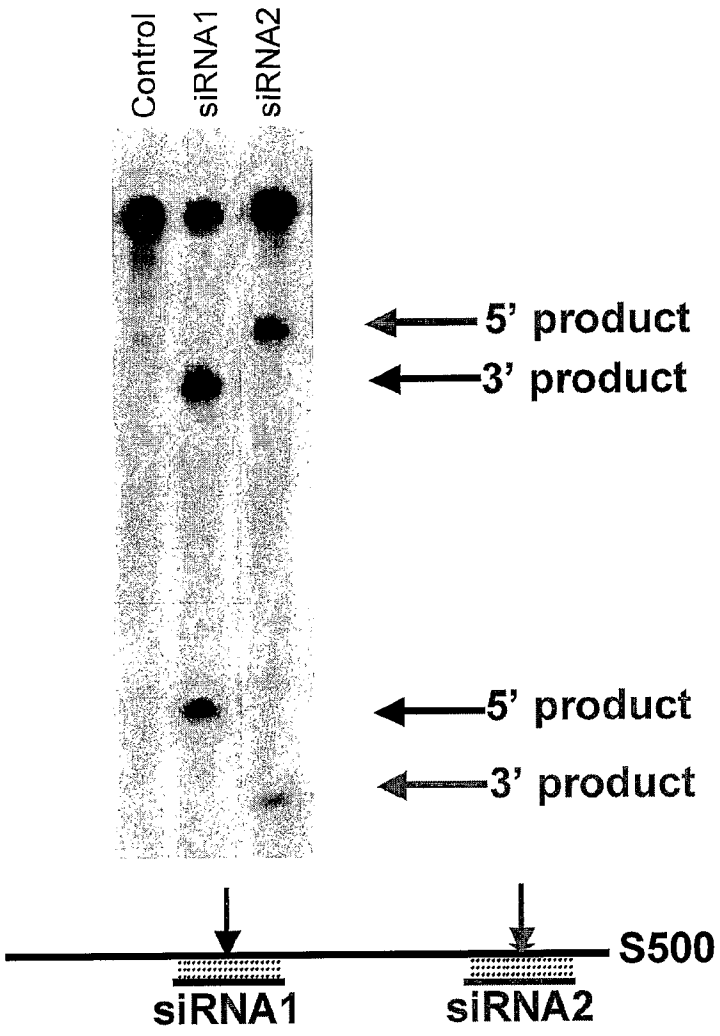
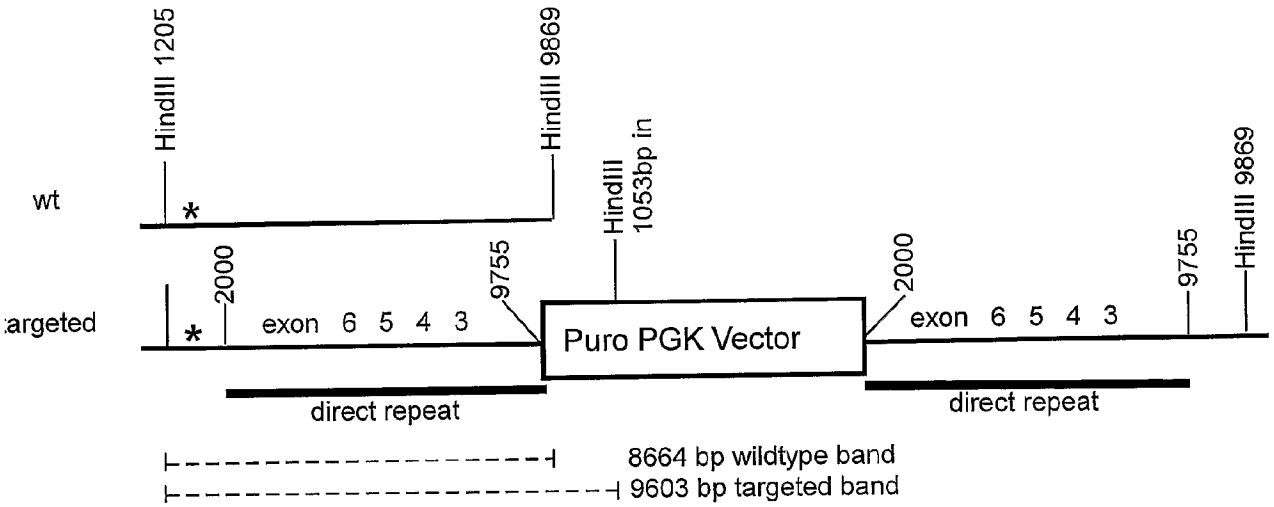

Control
siRNA1
siRNA2
5' product
3' product
5' product
3' product
S500
siRNA1
siRNA2

Figure 14


HindIII 1205
HindIII 9869
HindIII 1053bp in
wt
2000
9755
2000
9755
HindIII 9869
targeted
exon 6 5 4 3
Puro PGK Vector
exon 6 5 4 3
direct repeat
direct repeat
8664 bp wildtype band
9603 bp targeted band

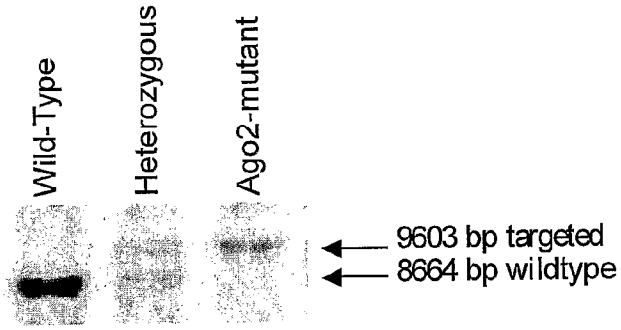

Wild-Type
Heterozygous
Ago2-mutant
9603 bp targeted
8664 bp wildtype

Figure 15

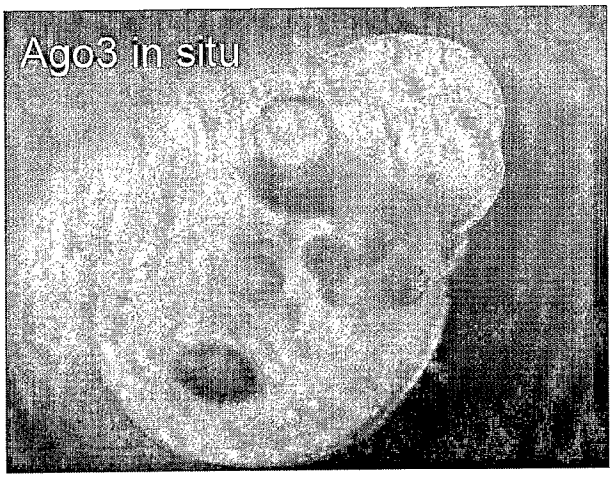


Figure 16

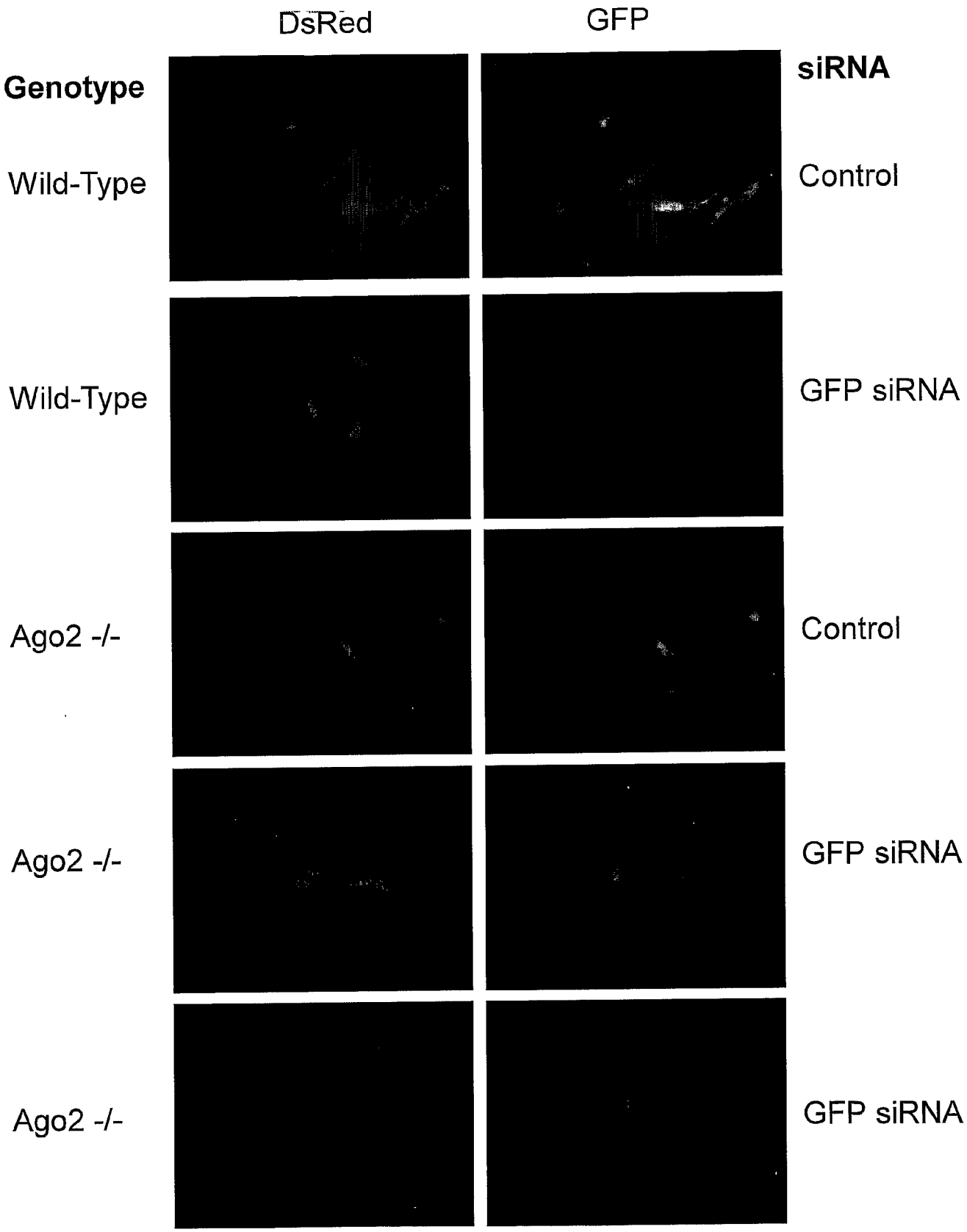

DsRed
GFP
Genotype
siRNA
Wild-Type
Control
Wild-Type
GFP siRNA
Ago2 -/-
Control
Ago2 -/-
GFP siRNA
Ago2 -/-
GFP siRNA

Figure 17

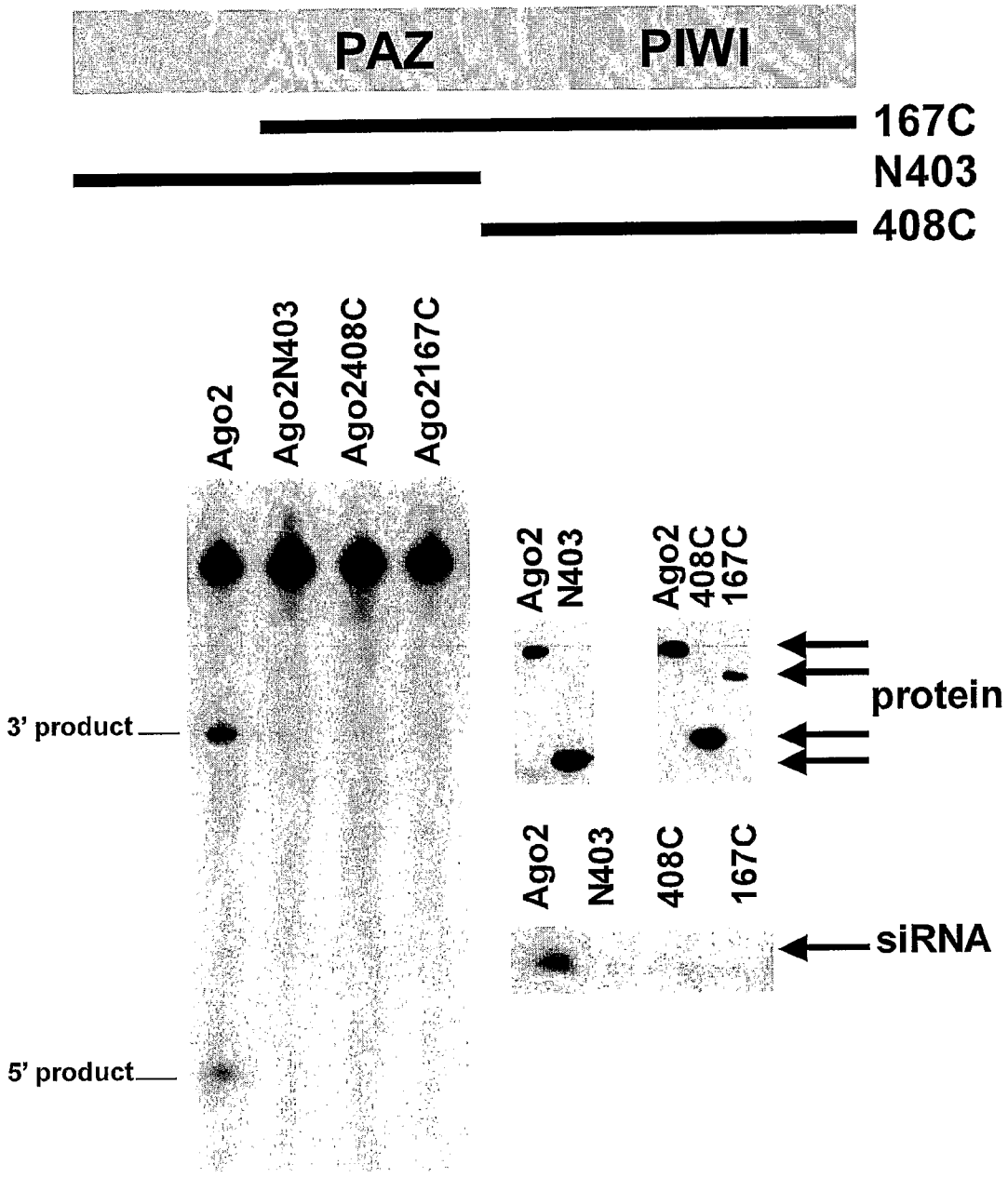

PAZ
PIWI
167C
N403
408C
Ago2
Ago2N403
Ago2408C
Ago2167C
3' product
5' product
Ago2
N403
Ago2
408C
167C
protein
Ago2
N403
408C
167C
siRNA

Figure 18

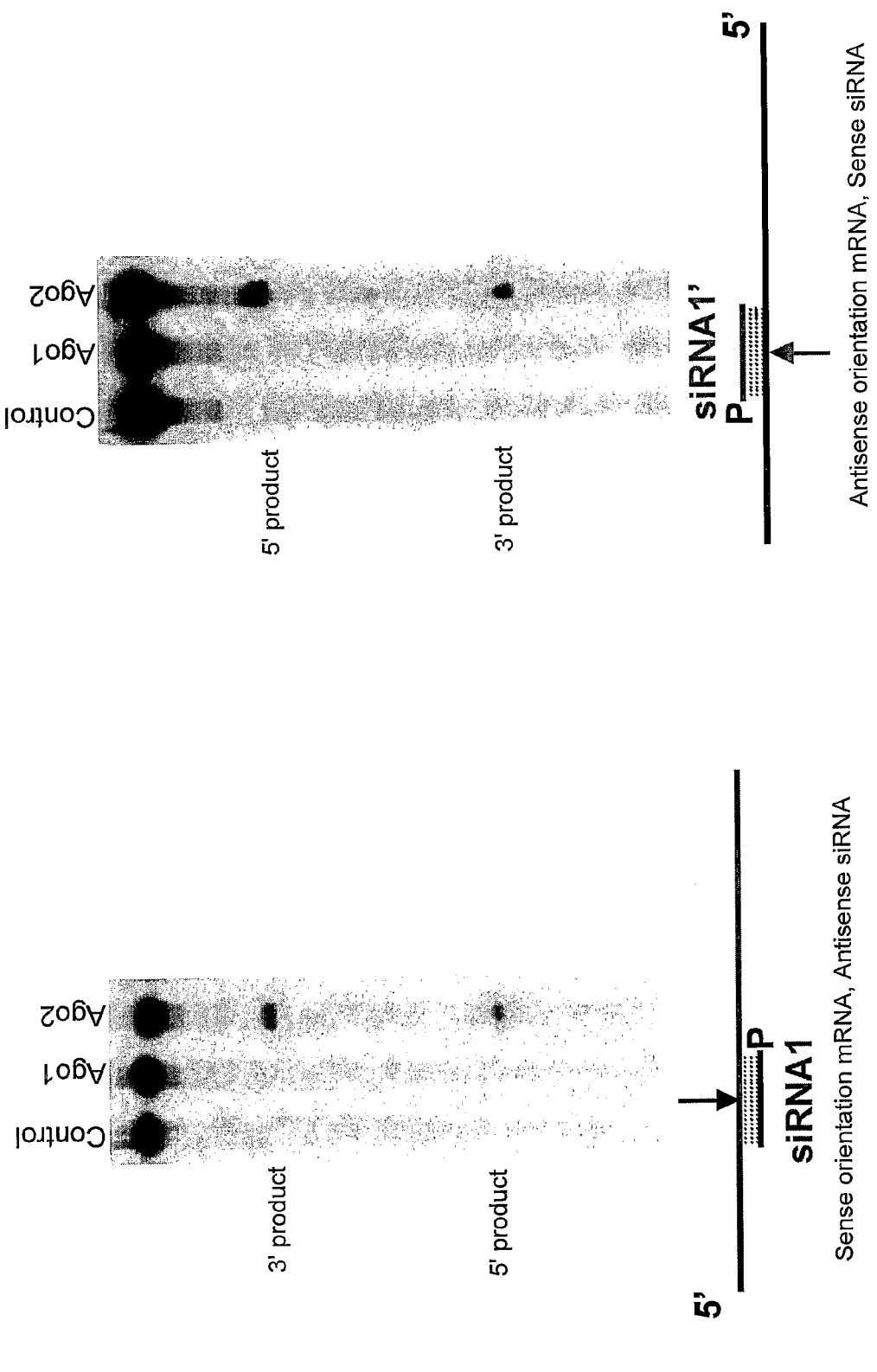

Control
Ago1
Ago2
3' product
5' product
5'
siRNA1
P
Sense orientation mRNA, Antisense siRNA
Control
Ago1
Ago2
5' product
3' product
5'
siRNA1'
P
Antisense orientation mRNA, Sense siRNA

Figure 19

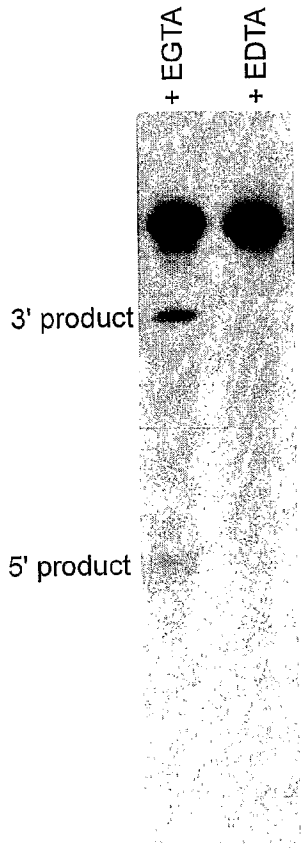


Figure 20

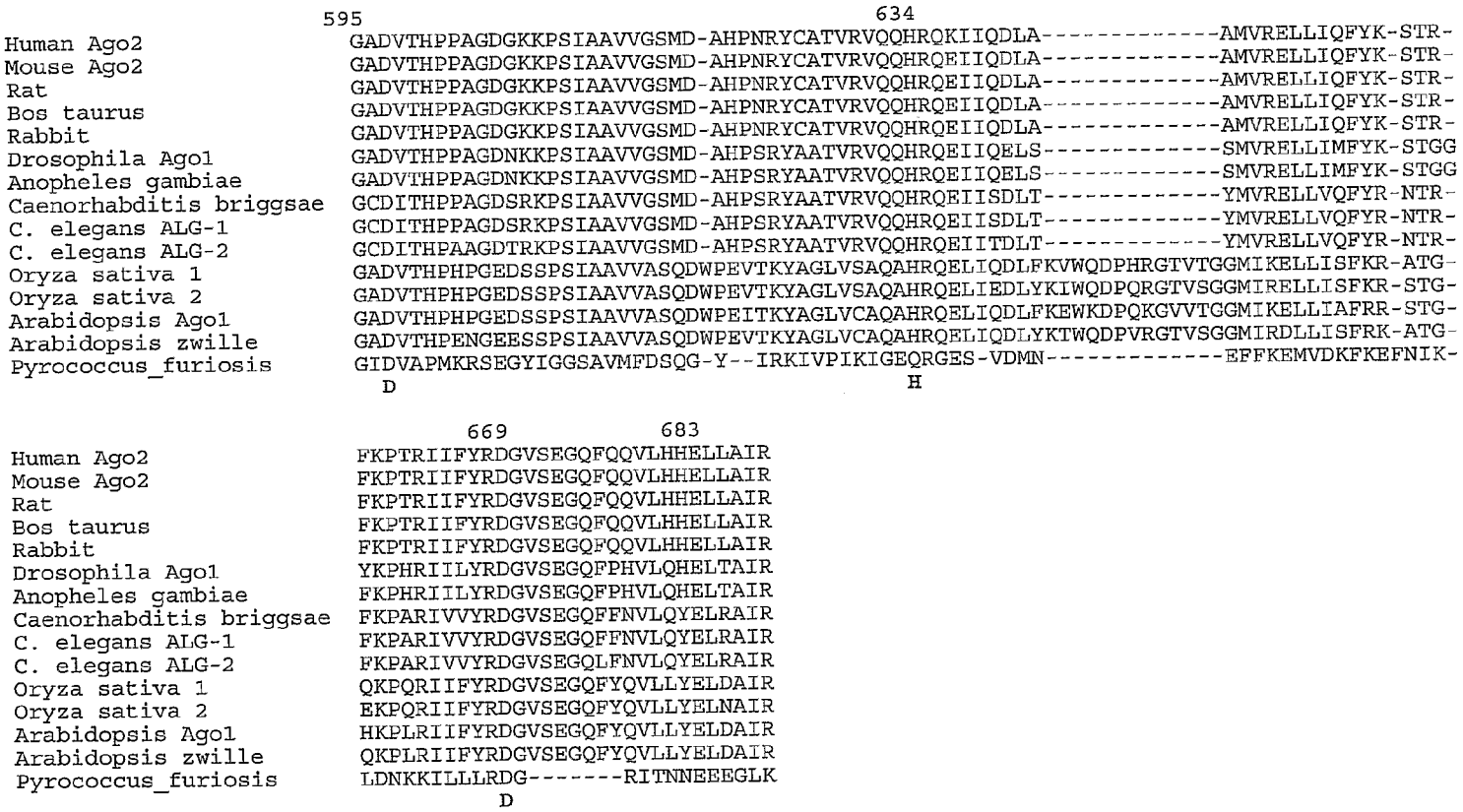

595
634
Human Ago2 GADVTHPPAGDGKKPSIAAVVGSMD-AHPNRYCATVRVQQHRQKIIQDLA----------AMVRELLIQFYK-STR-
Mouse Ago2 GADVTHPPAGDGKKPSIAAVVGSMD-AHPNRYCATVRVQQHRQEIIQDLA----------AMVRELLIQFYK-STR-
Rat GADVTHPPAGDGKKPSIAAVVGSMD-AHPNRYCATVRVQQHRQEIIQDLA----------AMVRELLIQFYK-STR-
Bos taurus GADVTHPPAGDGKKPSIAAVVGSMD-AHPNRYCATVRVQQHRQEIIQDLA----------AMVRELLIQFYK-STR-
Rabbit GADVTHPPAGDGKKPSIAAVVGSMD-AHPNRYCATVRVQQHRQEIIQDLA----------AMVRELLIQFYK-STR-
Drosophila Ago1 GADVTHPPAGDNKKPSIAAVVGSMD-AHPSRYAATVRVQQHRQEIIQELS----------SMVRELLIMFYK-STGG
Anopheles gambiae GADVTHPPAGDNKKPSIAAVVGSMD-AHPSRYAATVRVQQHRQEIIQELS----------SMVRELLIMFYK-STGG
Caenorhabditis briggsae GCDITHPPAGDSRKPSIAAVVGSMD-AHPSRYAATVRVQQHRQEIISDLT----------YMVRELLVQFYR-NTR-
C. elegans ALG-1 GCDITHPPAGDSRKPSIAAVVGSMD-AHPSRYAATVRVQQHRQEIISDLT----------YMVRELLVQFYR-NTR-
C. elegans ALG-2 GCDITHPAAGDTRKPSIAAVVGSMD-AHPSRYAATVRVQQHRQEIITDLT----------YMVRELLVQFYR-NTR-
Oryza sativa 1 GADVTHPHPGEDSSPSIAAVVASQDWPEVTKYAGLVSAQAHRQELIQDLFKVWQDPHRGTVTGGMIKELLISFKR-ATG-
Oryza sativa 2 GADVTHPHPGEDSSPSIAAVVASQDWPEVTKYAGLVSAQAHRQELIEDLYKIWQDPQRGTVSGGMIRELLISFKR-STG-
Arabidopsis Ago1 GADVTHPHPGEDSSPSIAAVVASQDWPEITKYAGLVCAQAHRQELIQDLFKEWKDPQKGVVTGGMIKELLIAFRR-STG-
Arabidopsis zwille GADVTHPENGEESSPSIAAVVASQDWPEVTKYAGLVCAQAHRQELIQDLYKTWQDPVRGTVSGGMIRDLLISFRK-ATG-
Pyrococcus_furiosis GIDVAPMKRSEGYIGGSAVMFDSQG-Y--IRKIVPIKIGEQRGES-VDMN----------EFFKEMVDKFKEFNIK-
D
H
669
683
Human Ago2 FKPTRIIFYRDGVSEGQFQQVLHHELLAIR
Mouse Ago2 FKPTRIIFYRDGVSEGQFQQVLHHELLAIR
Rat FKPTRIIFYRDGVSEGQFQQVLHHELLAIR
Bos taurus FKPTRIIFYRDGVSEGQFQQVLHHELLAIR
Rabbit FKPTRIIFYRDGVSEGQFQQVLHHELLAIR
Drosophila Ago1 YKPHRIILYRDGVSEGQFPHVLQHELTAIR
Anopheles gambiae FKPHRIILYRDGVSEGQFPHVLQHELTAIR
Caenorhabditis briggsae FKPARIVVYRDGVSEGQFFNVLQYELRAIR
C. elegans ALG-1 FKPARIVVYRDGVSEGQFFNVLQYELRAIR
C. elegans ALG-2 FKPARIVVYRDGVSEGQLFNVLQYELRAIR
Oryza sativa 1 QKPQRIIFYRDGVSEGQFYQVLLYELDAIR
Oryza sativa 2 EKPQRIIFYRDGVSEGQFYQVLLYELNAIR
Arabidopsis Ago1 HKPLRIIFYRDGVSEGQFYQVLLYELDAIR
Arabidopsis zwille QKPLRIIFYRDGVSEGQFYQVLLYELDAIR
Pyrococcus_furiosis LDNKKILLLRDG-------RITNNEEEGLK
D

Figure 21

Figure 22

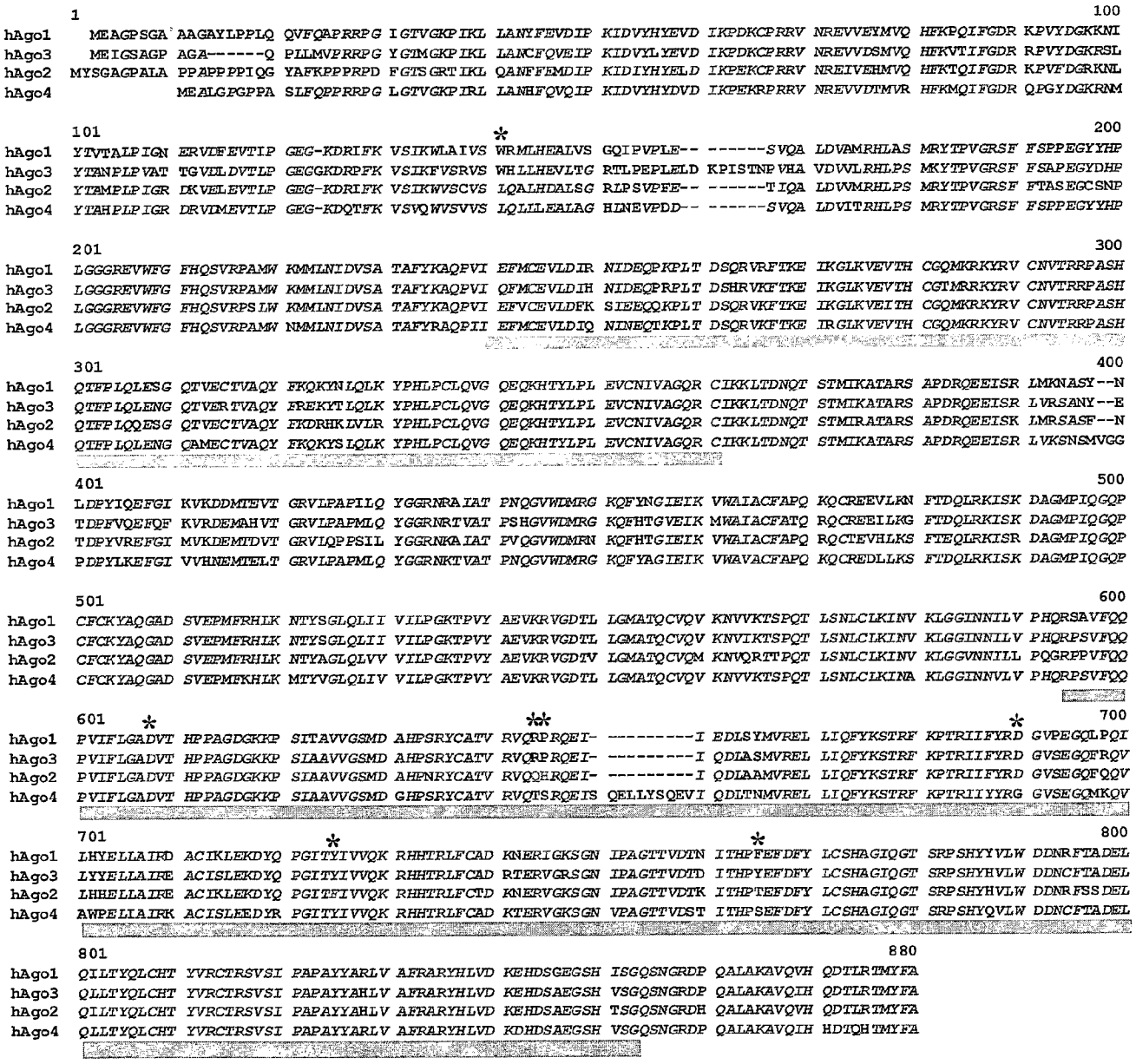

1 100
hAgo1 MEAGPSGA AAGAYLPPLQ QVFQAPRRPG IGTVGKPIKL LANYFEVDIP KIDVYHYEVD IKPDKCPRRV NREVVEYMVQ HFKPQIFGDR KPVYDGKKNI
hAgo3 MEIGSAGP AGA------Q PLLMVPRRPG YGTMGKPIKL LANCFQVEIP KIDVYLYEVD IKPDKCPRRV NREVVDSMVQ HFKVTIFGDR RPVYDGKRSL
hAgo2 MYSGAGPALA PPAPPPPIQG YAFKPPPRPD FGTSGRTIKL QANFFEMDIP KIDIYHYELD IKPEKCPRRV NREIVEHMVQ HFKTQIFGDR KPVFDGRKNL
hAgo4 MEALGPGPPA SLFQPPRRPG LGTVGKPIRL LANHFQVQIP KIDVYHYDVD IKPEKRPRRV NREVVDTMVR HFKMQIFGDR QPGYDGKRNM
101 200
hAgo1 YTVTALPIGN ERVDFEVTIP GEG-KDRIFK VSIKWLAIVS WRMLHEALVS GQIPVPLE-- ------SVQA LDVAMRHLAS MRYTPVGRSF FSPPEGYYHP
hAgo3 YTANPLPVAT TGVDLDVTLP GECGKDRPFK VSIKFVSRVS WHLLHEVLTG RTLPEPLELD KPISTNPVHA VDWLRHLPS MKYTPVGRSF FSAPEGYDHP
hAgo2 YTAMPLPIGR DKVELEVTLP GEG-KDRIFK VSIKWVSCVS LQALHDALSG RLPSVPFE-- ------TIQA LDVMRHLPS MRYTPVGRSF FTASEGCSNP
hAgo4 YTAHPLPIGR DRVDMEVTLP GEG-KDQTFK VSVQWVSVVS LQLLLEALAG HLNEVPDD-- ------SVQA LDVITRHLPS MRYTPVGRSF FSPPEGYYHP
201 300
hAgo1 LGGGREVWFG FHQSVRPAMW KMMLNIDVSA TAFYKAQPVI EFMCEVLDIR NIDEQPKPLT DSQRVRFTKE IKGLKVEVTH CGQMKRKYRV CNVTRRPASH
hAgo3 LGGGREVWFG FHQSVRPAMW KMMLNIDVSA TAFYKAQPVI QFMCEVLDIH NIDEQPRPLT DSHRVKFTKE IKGLKVEVTH CGTMRRKYRV CNVTRRPASH
hAgo2 LGGGREVWFG FHQSVRPSLW KMMLNIDVSA TAFYKAQPVI EFVCEVLDFK SIEEQQKPLT DSQRVKFTKE IKGLKVEITH CGQMKRKYRV CNVTRRPASH
hAgo4 LGGGREVWFG FHQSVRPAMW NMMLNIDVSA TAFYRAQPII EFMCEVLDIQ NINEQTKPLT DSQRVKFTKE IRGLKVEVTH CGQMKRKYRV CNVTRRPASH
301 400
hAgo1 QTFPLQLESG QTVECTVAQY FKQKYNLQLK YPHLPCLQVG QEQKHTYLPL EVCNIVAGQR CIKKLTDNQT STMIKATARS APDRQEEISR LMKNASY--N
hAgo3 QTFPLQLENG QTVERTVAQY FREKYTLQLK YPHLPCLQVG QEQKHTYLPL EVCNIVAGQR CIKKLTDNQT STMIKATARS APDRQEEISR LVRSANY--E
hAgo2 QTFPLQQESG QTVECTVAQY FKDRHKLVLR YPHLPCLQVG QEQKHTYLPL EVCNIVAGQR CIKKLTDNQT STMIRATARS APDRQEEISK LMRSASF--N
hAgo4 QTFPLQLENG QAMECTVAQY FKQKYSLQLK YPHLPCLQVG QEQKHTYLPL EVCNIVAGQR CIKKLTDNQT STMIKATARS APDRQEEISR LVKSNSMVGG
401 500
hAgo1 LDPYIQEFGI KVKDDMTEVT GRVLPAPILQ YGGRNRAIAT PNQGVWDMRG KQFYNGIEIK VWAIACFAPQ KQCREEVLKN FTDQLRKISK DAGMPIQGQP
hAgo3 TDPFVQEFQF KVRDEMAHVT GRVLPAPMLQ YGGRNRTVAT PSHGVWDMRG KQFHTGVEIK MWAIACFATQ RQCREEILKG FTDQLRKISK DAGMPIQGQP
hAgo2 TDPYVREFGI MVKDEMTDVT GRVLQPPSIL YGGRNKAIAT PVQGVWDMRN KQFHTGIEIK VWAIACFAPQ RQCTEVHLKS FTEQLRKISR DAGMPIQGQP
hAgo4 PDPYLKEFGI VVHNEMTELT GRVLPAPMLQ YGGRNKTVAT PNQGVWDMRG KQFYAGIEIK VWAVACFAPQ KQCREDLLKS FTDQLRKISK DAGMPIQGQP
501 600
hAgo1 CFCKYAQGAD SVEPMFRHLK NTYSGLQLII VILPGKTPVY AEVKRVGDTL LGMATQCVQV KNVVKTSPQT LSNLCLKINV KLGGINNILV PHQRSAVFQQ
hAgo3 CFCKYAQGAD SVEPMFRHLK NTYSGLQLII VILPGKTPVY AEVKRVGDTL LGMATQCVQV KNVIKTSPQT LSNLCLKINV KLGGINNILV PHQRPSVFQQ
hAgo2 CFCKYAQGAD SVEPMFRHLK NTYAGLQLVV VILPGKTPVY AEVKRVGDTV LGMATQCVQM KNVQRTTPQT LSNLCLKINV KLGGVNNILL PQGRPPVFQQ
hAgo4 CFCKYAQGAD SVEPMFKHLK MTYVGLQLIV VILPGKTPVY AEVKRVGDTL LGMATQCVQV KNVVKTSPQT LSNLCLKINA KLGGINNVLV PHQRPSVFQQ
601 700
hAgo1 PVIFLGADVT HPPAGDGKKP SITAVVGSMD AHPSRYCATV RVQRPRQEI- ----------I EDLSYMVREL LIQFYKSTRF KPTRIIFYRD GVPEGQLPQI
hAgo3 PVIFLGADVT HPPAGDGKKP SIAAVVGSMD AHPSRYCATV RVQRPRQEI- ----------I QDIASMVREL LIQFYKSTRF KPTRIIFYRD GVSEGQFRQV
hAgo2 PVIFLGADVT HPPAGDGKKP SIAAVVGSMD AHPNRYCATV RVQQHRQEI- ----------I QDIAAMVREL LIQFYKSTRF KPTRIIFYRD GVSEGQFQQV
hAgo4 PVIFLGADVT HPPAGDGKKP SIAAVVGSMD GHPSRYCATV RVQTSRQEIS QELLYSQEVI QDLTNMVREL LIQFYKSTRF KPTRIIYYRG GVSEGQMKQV
701 800
hAgo1 LHYELLAIRD ACIKLEKDYQ PGITYIVVQK RHHTRLFCAD KNERIGKSGN IPAGTTVDTN ITHPFEFDFY LCSHAGIQGT SRPSHYYVLW DDNRFTADEL
hAgo3 LYYELLAIRE ACISLEKDYQ PGITYIVVQK RHHTRLFCAD RTERVGRSGN IPAGTTVDTD ITHPYEFDFY LCSHAGIQGT SRPSHYHVLW DDNCFTADEL
hAgo2 LHHELLAIRE ACIKLEKDYQ PGITFIVVQK RHHTRLFCTD KNERVGKSGN IPAGTTVDTK ITHPTEFDFY LCSHAGIQGT SRPSHYHVLW DDNRFSSDEL
hAgo4 AWPELIAIRK ACISLEEDYR PGITYIVVQK RHHTRLFCAD KTERVGKSGN VPAGTTVDST ITHPSEFDFY LCSHAGIQGT SRPSHYQVLW DDNCFTADEL
801 880
hAgo1 QILTYQLCHT YVRCTRSVSI PAPAYYARLV AFRARYHLVD KEHDSGEGSH ISGQSNGRDP QALAKAVQVH QDTLRTMYFA
hAgo3 QLLTYQLCHT YVRCTRSVSI PAPAYYAHLV AFRARYHLVD KEHDSAEGSH VSGQSNGRDP QALAKAVQIH QDTLRTMYFA
hAgo2 QILTYQLCHT YVRCTRSVSI PAPAYYAHLV AFRARYHLVD KEHDSAEGSH TSGQSNGRDH QALAKAVQVH QDTLRTMYFA
hAgo4 QLLTYQLCHT YVRCTRSVSI PAPAYYARLV AFRARYHLVD KDHDSAEGSH VSGQSNGRDP QALAKAVQIH HDTQHTMYFA

Figure 23

Table 1. Crystallographic Statistics

Space group	$P2_1$
Unit cell	a=69.72, b=104.19, c=74.01, α=90, β=102.83, γ=90

A. Data Reduction Statistics

	λ(Å)	Resolution(Å)	Measured Reflections	Unique Reflections	Percent Complete	I/σ(I)	R_{sym}[a]
Se peak	0.9791	2.25(2.33-2.25)	350855	48108(4820)	98.7(100)	42.6(6.03)	0.078(0.473)
Se edge	0.9796	2.25(2.33-2.25)	351677	48228(4852)	98.7(100)	41.8(5.50)	0.060(0.511)
Se remote	0.9638	2.25(2.33-2.25)	354296	48470(4848)	99.3(100)	41.6(4.34)	0.066(0.632)
Hg peak	1.0076	2.25(2.33-2.25)	354357	48293(4781)	99.8(100)	39.4(4.24)	0.086(0.666)

B. Phasing Statistics

	Acentric Phasing Power[b]		Centric Phasing Power	
	50-2.25Å	2.31-2.25Å	50-2.25Å	2.31-2.25Å
Se peak anomalous	2.912	0.616		
Se edge isomorphous	0.903	0.294	0.690	0.212
Se edge anomalous	1.234	0.267		
Se remote isomorphous	0.598	0.191	0.458	0.313
Se remote anomalous	1.389	0.313		
Hg peak isomorphous	0.801	0.406	0.717	0.331
Hg peak anomalous	0.301	0.069		

FOM[c]	50-2.25 Å	2.31-2.25 Å
Accentric reflections	0.553	0.305
Centric reflections	0.305	0.177

C. Refinement Statistics

Reflection used	500-2.25 Å
Number of atoms	5990(protein:5913, water:77)
R_{work}/#ref	0.2420/46298
R_{free}/#ref	0.2708/2528

D. Geometry

	Core	Allowed
Ramachandran plot(%)	84.2	15.8
Bond length RMSD(Å)	0.0066	
Bond angle RMSD( )	1.273	

[a] R_{sym};$R_{ano} = \sum|I-\langle I\rangle|/\sum(I)$, calculated by retaining anomalous-mates and symmetry-mates as independent observations, respectively.
[b] Phasing power calculated as F_H(calc)phase integrated lack of closure.
[c] FOM is weighted over F amplitude and phase as calculated by the program SHARP.

Figure 24

Table 2. Crystallographic Statistics

Space group	$P2_1$
Unit cell	a=69.72, b=104.19, c=74.01, α=90, β=102.83, γ=90

A. Data Reduction Statistics

	λ(Å)	Resolution(Å)	Measured Reflections	Unique Reflections	Percent Complete	I/σ(I)
Se peak	0.9791	2.25(2.33-2.25)	350855	48108(4820)	98.7(100)	42.6(6.03)
Se edge	0.9796	2.25(2.33-2.25)	351677	48228(4852)	98.7(100)	41.8(5.50)
Se remote	0.9638	2.25(2.33-2.25)	354296	48470(4848)	99.3(100)	41.6(4.34)
Hg peak	1.0076	2.25(2.33-2.25)	354357	48293(4781)	99.8(100)	39.4(4.24)

B. Phasing Statistics

	Acentric Phasing Power[b]		Centric Phasing Power	
	50-2.25Å	2.31-2.25Å	50-2.25Å	2.31-2.25Å
Se peak anomalous	2.912	0.616		
Se edge isomorphous	0.903	0.294	0.690	0.212
Se edge anomalous	1.234	0.267		
Se remote isomorphous	0.598	0.191	0.458	0.313
Se remote anomalous	1.389	0.313		
Hg peak isomorphous	0.801	0.406	0.717	0.331
Hg peak anomalous	0.301	0.069		

FOM[c]	50-2.25 Å	2.31-2.25 Å
Accentric reflections	0.553	0.305
Centric reflections	0.305	0.177

C. Refinement Statistics

Reflection used	38.14-2.25 Å
Number of atoms	6113(protein:5921, water:192)
R_{work}/#ref	0.228/46294
R_{free}/#ref	0.258/2528

D. Geometry

	Core	Allowed
Ramachandran plot(%)	85.6	14.4

Bond length RMSD(Å)	0.0064
Bond angle RMSD( )	1.217

[a] R_{sym};$R_{ano} = \sum|I-\langle I\rangle|/\sum(I)$, calculated by retaining anomalous-mates and symmetry-mates as independent observations, respectively.
[b] Phasing power calculated as F_H(calc)phase integrated lack of closure.
[c] FOM is weighted over F amplitude and phase as calculated by the program SHARP.

Table 3

```
REMARK   3
REMARK   3 REFINEMENT.
REMARK   3   PROGRAM     : CNS 1.1
REMARK   3   AUTHORS     : BRUNGER, ADAMS, CLORE, DELANO,
REMARK   3                 GROS, GROSSE-KUNSTLEVE, JIANG,
REMARK   3                 KUSZEWSKI, NILGES, PANNU, READ,
REMARK   3                 RICE, SIMONSON, WARREN
REMARK   3
REMARK   3  DATA USED IN REFINEMENT.
REMARK   3   RESOLUTION RANGE HIGH (ANGSTROMS) : 2.25
REMARK   3   RESOLUTION RANGE LOW  (ANGSTROMS) :  38.17
REMARK   3   DATA CUTOFF            (SIGMA(F)) : 0.0
REMARK   3   DATA CUTOFF HIGH         (ABS(F)) :  1695436.78
REMARK   3   DATA CUTOFF LOW          (ABS(F)) :    0.000000
REMARK   3   COMPLETENESS (WORKING+TEST)   (%) : 99.7
REMARK   3   NUMBER OF REFLECTIONS             : 48822
REMARK   3
REMARK   3  FIT TO DATA USED IN REFINEMENT.
REMARK   3   CROSS-VALIDATION METHOD           : THROUGHOUT
REMARK   3   FREE R VALUE TEST SET SELECTION   : RANDOM
REMARK   3   R VALUE            (WORKING SET) : 0.227
REMARK   3   FREE R VALUE                      : 0.258
REMARK   3   FREE R VALUE TEST SET SIZE   (%) :  5.2
REMARK   3   FREE R VALUE TEST SET COUNT       :  2528
REMARK   3   ESTIMATED ERROR OF FREE R VALUE   : 0.005
REMARK   3
REMARK   3  FIT IN THE HIGHEST RESOLUTION BIN.
REMARK   3   TOTAL NUMBER OF BINS USED           :   6
REMARK   3   BIN RESOLUTION RANGE HIGH       (A) : 2.25
REMARK   3   BIN RESOLUTION RANGE LOW        (A) : 2.39
REMARK   3   BIN COMPLETENESS (WORKING+TEST) (%) :100.0
REMARK   3   REFLECTIONS IN BIN    (WORKING SET) :  7694
REMARK   3   BIN R VALUE           (WORKING SET) : 0.295
REMARK   3   BIN FREE R VALUE                    : 0.350
REMARK   3   BIN FREE R VALUE TEST SET SIZE  (%) :  5.2
REMARK   3   BIN FREE R VALUE TEST SET COUNT     :   422
REMARK   3   ESTIMATED ERROR OF BIN FREE R VALUE : 0.017
REMARK   3
REMARK   3  NUMBER OF NON-HYDROGEN ATOMS USED IN REFINEMENT.
REMARK   3   PROTEIN ATOMS            : 5920
REMARK   3   NUCLEIC ACID ATOMS       :    0
REMARK   3   HETEROGEN ATOMS          :    0
REMARK   3   SOLVENT ATOMS            :  192
REMARK   3
REMARK   3  B VALUES.
REMARK   3   FROM WILSON PLOT           (A**2) : 39.1
REMARK   3   MEAN B VALUE      (OVERALL, A**2) : 63.9
REMARK   3   OVERALL ANISOTROPIC B VALUE.
REMARK   3    B11 (A**2) : -7.73
REMARK   3    B22 (A**2) :  1.12
REMARK   3    B33 (A**2) :  6.61
REMARK   3    B12 (A**2) :  0.00
REMARK   3    B13 (A**2) : -7.39
REMARK   3    B23 (A**2) :  0.00
```

FIGURE 25

```
REMARK   3
REMARK   3  BULK SOLVENT MODELING.
REMARK   3   METHOD USED : FLAT MODEL
REMARK   3   KSOL        : 0.327326
REMARK   3   BSOL        : 55.1711 (A**2)
REMARK   3
REMARK   3  ESTIMATED COORDINATE ERROR.
REMARK   3   ESD FROM LUZZATI PLOT        (A) : 0.32
REMARK   3   ESD FROM SIGMAA              (A) : 0.27
REMARK   3   LOW RESOLUTION CUTOFF        (A) : 5.00
REMARK   3
REMARK   3  CROSS-VALIDATED ESTIMATED COORDINATE ERROR.
REMARK   3   ESD FROM C-V LUZZATI PLOT    (A) : 0.37
REMARK   3   ESD FROM C-V SIGMAA          (A) : 0.36
REMARK   3
REMARK   3  RMS DEVIATIONS FROM IDEAL VALUES.
REMARK   3   BOND LENGTHS                 (A) : 0.007
REMARK   3   BOND ANGLES            (DEGREES) : 1.2
REMARK   3   DIHEDRAL ANGLES        (DEGREES) : 22.7
REMARK   3   IMPROPER ANGLES        (DEGREES) : 0.76
REMARK   3

REMARK   3  ISOTROPIC THERMAL MODEL : GROUP
REMARK   3
REMARK   3  ISOTROPIC THERMAL FACTOR RESTRAINTS.     RMS     SIGMA
REMARK   3   MAIN-CHAIN BOND              (A**2) : NULL  ; NULL
REMARK   3   MAIN-CHAIN ANGLE             (A**2) : NULL  ; NULL
REMARK   3   SIDE-CHAIN BOND              (A**2) : NULL  ; NULL
REMARK   3   SIDE-CHAIN ANGLE             (A**2) : NULL  ; NULL
REMARK   3
REMARK   3  NCS MODEL : NONE
REMARK   3
REMARK   3  NCS RESTRAINTS.                          RMS   SIGMA/WEIGHT
REMARK   3   GROUP  1  POSITIONAL            (A) : NULL  ; NULL
REMARK   3   GROUP  1  B-FACTOR           (A**2) : NULL  ; NULL
REMARK   3
REMARK   3  PARAMETER FILE  1  : CNS_TOPPAR/protein_rep.param
REMARK   3  PARAMETER FILE  2  : CNS_TOPPAR/water_rep.param
REMARK   3  TOPOLOGY FILE  1   : CNS_TOPPAR/protein.top
REMARK   3  TOPOLOGY FILE  2   : CNS_TOPPAR/water.top
REMARK   3
REMARK   3  OTHER REFINEMENT REMARKS: NULL
SEQRES   1 A  713  SER MSE LYS ALA ILE VAL VAL ILE ASN LEU VAL LYS ILE
SEQRES   2 A  713  ASN LYS LYS ILE ILE PRO ASP LYS ILE TYR VAL TYR ARG
SEQRES   3 A  713  LEU TYR SER ILE TYR ARG LEU ALA TYR GLU ASN VAL GLY
SEQRES   4 A  713  ILE VAL ILE ASP PRO GLU ASN LEU ILE ILE ALA THR THR
SEQRES   5 A  713  LYS GLU LEU GLU TYR GLU GLY GLU PHE ILE PRO GLU GLY
SEQRES   6 A  713  GLU ILE SER PHE SER GLU LEU ARG ASN ASP TYR GLN SER
SEQRES   7 A  713  LYS LEU VAL LEU ARG LEU LEU LYS GLU ASN GLY ILE GLY
SEQRES   8 A  713  GLU TYR GLU LEU SER LYS LEU LEU ARG LYS PHE ARG LYS
SEQRES   9 A  713  PRO LYS THR PHE GLY ASP TYR LYS VAL ILE PRO SER VAL
SEQRES  10 A  713  GLU MSE SER VAL ILE LYS HIS ASP GLU ASP PHE TYR LEU
SEQRES  11 A  713  VAL ILE HIS ILE ILE HIS GLN ILE GLN SER MSE LYS THR
SEQRES  12 A  713  LEU TRP GLU LEU VAL ASN LYS ASP PRO LYS GLU LEU GLU
SEQRES  13 A  713  GLU PHE LEU MSE THR HIS LYS GLU ASN LEU MSE LEU LYS
SEQRES  14 A  713  ASP ILE ALA SER PRO LEU LYS THR VAL TYR LYS PRO CYS
```

```
SEQRES  15 A  713  PHE GLU GLU TYR THR LYS LYS PRO LYS LEU ASP HIS ASN
SEQRES  16 A  713  GLN GLU ILE VAL LYS TYR TRP TYR ASN TYR HIS ILE GLU
SEQRES  17 A  713  ARG TYR TRP ASN THR PRO GLU ALA LYS LEU GLU PHE TYR
SEQRES  18 A  713  ARG LYS PHE GLY GLN VAL ASP LEU LYS GLN PRO ALA ILE
SEQRES  19 A  713  LEU ALA LYS PHE ALA SER LYS ASN TYR LYS ILE TYR LEU
SEQRES  20 A  713  LEU PRO GLN LEU VAL VAL PRO THR TYR ASN ALA GLU GLN
SEQRES  21 A  713  LEU ALA LYS GLU ILE LEU GLU TYR THR LYS LEU MSE PRO
SEQRES  22 A  713  GLU GLU ARG LYS GLU LEU LEU GLU ASN ILE LEU ALA GLU
SEQRES  23 A  713  VAL ASP SER ASP ILE ILE ASP LYS SER LEU SER GLU ILE
SEQRES  24 A  713  GLU VAL GLU LYS ILE ALA GLN GLU LEU GLU ASN LYS ILE
SEQRES  25 A  713  ARG VAL ARG ASP ASP LYS GLY ASN SER VAL PRO ILE SER
SEQRES  26 A  713  GLN LEU LEU TRP THR ASN TYR SER ARG LYS TYR PRO VAL

SEQRES  27 A  713  ILE LEU PRO TYR GLU VAL PRO GLU LYS PHE ARG LYS ILE
SEQRES  28 A  713  ARG GLU ILE PRO MSE PHE ILE ILE LEU ASP SER GLY LEU
SEQRES  29 A  713  LEU ALA ASP ILE GLN ASN PHE ALA THR ASN GLU PHE ARG
SEQRES  30 A  713  GLU LEU VAL LYS SER MSE TYR TYR GLU LYS VAL ILE THR
SEQRES  31 A  713  GLU ASP LEU ASN SER ASP LYS GLY ILE ILE GLU VAL VAL
SEQRES  32 A  713  GLU GLN VAL SER SER PHE MSE LYS GLY LYS GLU LEU GLY
SEQRES  33 A  713  LEU ALA PHE ILE ALA ALA ARG ASN LYS LEU SER SER GLU
SEQRES  34 A  713  LYS PHE GLU GLU ILE LYS ARG ARG LEU PHE ASN LEU ASN
SEQRES  35 A  713  VAL ILE SER GLN VAL VAL ASN GLU ASP THR LEU LYS ASN
SEQRES  36 A  713  LYS ARG ASP LYS TYR ASP ARG ASN ARG LEU ASP LEU PHE
SEQRES  37 A  713  VAL ARG HIS ASN LEU LEU PHE GLN VAL LEU SER LYS LEU
SEQRES  38 A  713  GLY VAL LYS TYR TYR VAL LEU ASP TYR ARG PHE ASN TYR
SEQRES  39 A  713  ASP TYR ILE ILE GLY ILE ASP VAL ALA PRO MSE LYS ARG
SEQRES  40 A  713  SER GLU GLY TYR ILE GLY GLY SER ALA VAL MSE PHE ASP
SEQRES  41 A  713  SER GLN GLY TYR ILE ARG LYS ILE VAL PRO ILE LYS ILE
SEQRES  42 A  713  GLY GLU GLN ARG GLY GLU SER VAL ASP MSE ASN GLU PHE
SEQRES  43 A  713  PHE LYS GLU MSE VAL ASP LYS PHE LYS GLU PHE ASN ILE
SEQRES  44 A  713  LYS LEU ASP ASN LYS LYS ILE LEU LEU LEU ARG ASP GLY
SEQRES  45 A  713  ARG ILE THR ASN ASN GLU GLU GLU GLY LEU LYS TYR ILE
SEQRES  46 A  713  SER GLU MSE PHE ASP ILE GLU VAL VAL THR MSE ASP VAL
SEQRES  47 A  713  ILE LYS ASN HIS PRO VAL ARG ALA PHE ALA ASN MSE LYS
SEQRES  48 A  713  MSE TYR PHE ASN LEU GLY GLY ALA ILE TYR LEU ILE PRO
SEQRES  49 A  713  HIS LYS LEU LYS GLN ALA LYS GLY THR PRO ILE PRO ILE
SEQRES  50 A  713  LYS LEU ALA LYS LYS ARG ILE ILE LYS ASN GLY LYS VAL
SEQRES  51 A  713  GLU LYS GLN SER ILE THR ARG GLN ASP VAL LEU ASP ILE
SEQRES  52 A  713  PHE ILE LEU THR ARG LEU ASN TYR GLY SER ILE SER ALA
SEQRES  53 A  713  ASP MSE ARG LEU PRO ALA PRO VAL HIS TYR ALA HIS LYS
SEQRES  54 A  713  PHE ALA ASN ALA ILE ARG ASN GLU TRP LYS ILE LYS GLU
SEQRES  55 A  713  GLU PHE LEU ALA GLU GLY PHE LEU TYR PHE VAL
CRYST1   69.726  104.188   74.015  90.00 102.83  90.00 P 21          2
ORIGX1      1.000000  0.000000  0.000000        0.00000
ORIGX2      0.000000  1.000000  0.000000        0.00000
ORIGX3      0.000000  0.000000  1.000000        0.00000
SCALE1      0.014342  0.000000  0.003265        0.00000
SCALE2      0.000000  0.009598  0.000000        0.00000
SCALE3      0.000000  0.000000  0.013857        0.00000
ATOM      1  CB  SER A   0      -9.237  31.412  15.695  1.00 52.89      A
ATOM      2  OG  SER A   0      -9.737  30.155  16.110  1.00 52.89      A
ATOM      3  C   SER A   0     -10.483  32.911  17.228  1.00 79.00      A
ATOM      4  O   SER A   0     -10.625  34.075  17.612  1.00 79.00      A
ATOM      5  N   SER A   0      -8.485  31.638  18.031  1.00 79.00      A
ATOM      6  CA  SER A   0      -9.110  32.356  16.883  1.00 79.00      A
ATOM      7  N   MSE A   1     -11.494  32.061  17.086  1.00 80.16      A
ATOM      8  CA  MSE A   1     -12.873  32.436  17.365  1.00 80.16      A
```

```
ATOM      9  CB  MSE A   1     -13.792  31.773  16.330  1.00148.49      A
ATOM     10  CG  MSE A   1     -15.277  32.075  16.475  1.00148.49      A
ATOM     11  SE  MSE A   1     -15.681  33.960  16.497  1.00148.49      A
ATOM     12  CE  MSE A   1     -16.904  33.999  17.989  1.00148.49      A
ATOM     13  C   MSE A   1     -13.266  32.013  18.780  1.00 80.16      A
ATOM     14  O   MSE A   1     -12.455  31.466  19.529  1.00 80.16      A
ATOM     15  N   LYS A   2     -14.514  32.287  19.141  1.00 61.75      A
ATOM     16  CA  LYS A   2     -15.048  31.929  20.442  1.00 61.75      A
ATOM     17  CB  LYS A   2     -15.945  33.044  20.970  1.00 71.24      A
ATOM     18  CG  LYS A   2     -15.274  34.401  21.005  1.00 71.24      A
ATOM     19  CD  LYS A   2     -16.202  35.452  21.576  1.00 71.24      A
ATOM     20  CE  LYS A   2     -15.521  36.806  21.662  1.00 71.24      A
ATOM     21  NZ  LYS A   2     -16.416  37.829  22.282  1.00 71.24      A
ATOM     22  C   LYS A   2     -15.860  30.656  20.264  1.00 61.75      A
ATOM     23  O   LYS A   2     -16.065  30.196  19.139  1.00 61.75      A
ATOM     24  N   ALA A   3     -16.313  30.076  21.370  1.00 49.57      A
ATOM     25  CA  ALA A   3     -17.103  28.864  21.295  1.00 49.57      A
ATOM     26  CB  ALA A   3     -16.203  27.673  21.016  1.00 38.38      A
ATOM     27  C   ALA A   3     -17.859  28.681  22.597  1.00 49.57      A

ATOM     28  O   ALA A   3     -17.505  29.269  23.618  1.00 49.57      A
ATOM     29  N   ILE A   4     -18.921  27.885  22.552  1.00 48.74      A
ATOM     30  CA  ILE A   4     -19.728  27.632  23.736  1.00 48.74      A
ATOM     31  CB  ILE A   4     -21.239  27.735  23.437  1.00 52.34      A
ATOM     32  CG2 ILE A   4     -22.021  27.720  24.743  1.00 52.34      A
ATOM     33  CG1 ILE A   4     -21.545  29.034  22.677  1.00 52.34      A
ATOM     34  CD1 ILE A   4     -21.149  30.289  23.415  1.00 52.34      A
ATOM     35  C   ILE A   4     -19.433  26.223  24.218  1.00 48.74      A
ATOM     36  O   ILE A   4     -19.513  25.259  23.454  1.00 48.74      A
ATOM     37  N   VAL A   5     -19.075  26.103  25.489  1.00 41.68      A
ATOM     38  CA  VAL A   5     -18.775  24.794  26.033  1.00 41.68      A
ATOM     39  CB  VAL A   5     -17.244  24.619  26.297  1.00 47.32      A
ATOM     40  CG1 VAL A   5     -16.454  25.009  25.056  1.00 47.32      A
ATOM     41  CG2 VAL A   5     -16.802  25.455  27.483  1.00 47.32      A
ATOM     42  C   VAL A   5     -19.536  24.607  27.328  1.00 41.68      A
ATOM     43  O   VAL A   5     -19.790  25.565  28.051  1.00 41.68      A
ATOM     44  N   VAL A   6     -19.922  23.369  27.597  1.00 42.89      A
ATOM     45  CA  VAL A   6     -20.622  23.041  28.824  1.00 42.89      A
ATOM     46  CB  VAL A   6     -21.432  21.730  28.673  1.00 36.57      A
ATOM     47  CG1 VAL A   6     -22.045  21.327  30.019  1.00 36.57      A
ATOM     48  CG2 VAL A   6     -22.532  21.925  27.614  1.00 36.57      A
ATOM     49  C   VAL A   6     -19.549  22.824  29.882  1.00 42.89      A
ATOM     50  O   VAL A   6     -18.499  22.236  29.591  1.00 42.89      A
ATOM     51  N   ILE A   7     -19.802  23.308  31.095  1.00 41.08      A
ATOM     52  CA  ILE A   7     -18.856  23.138  32.197  1.00 41.08      A
ATOM     53  CB  ILE A   7     -18.278  24.496  32.676  1.00 37.86      A
ATOM     54  CG2 ILE A   7     -17.298  25.030  31.642  1.00 37.86      A
ATOM     55  CG1 ILE A   7     -19.418  25.475  32.948  1.00 37.86      A
ATOM     56  CD1 ILE A   7     -19.007  26.725  33.697  1.00 37.86      A
ATOM     57  C   ILE A   7     -19.595  22.476  33.346  1.00 41.08      A
ATOM     58  O   ILE A   7     -20.830  22.460  33.353  1.00 41.08      A
ATOM     59  N   ASN A   8     -18.847  21.949  34.318  1.00 40.94      A
ATOM     60  CA  ASN A   8     -19.443  21.253  35.460  1.00 40.94      A
ATOM     61  CB  ASN A   8     -18.456  20.201  36.002  1.00 34.10      A
ATOM     62  CG  ASN A   8     -17.200  20.807  36.637  1.00 34.10      A
ATOM     63  OD1 ASN A   8     -16.866  21.979  36.429  1.00 34.10      A
ATOM     64  ND2 ASN A   8     -16.487  19.988  37.404  1.00 34.10      A
```

FIGURE 25 CON'T

```
ATOM     65  C   ASN A   8     -19.989  22.120  36.602  1.00 40.94      A
ATOM     66  O   ASN A   8     -19.796  21.815  37.781  1.00 40.94      A
ATOM     67  N   LEU A   9     -20.689  23.190  36.239  1.00 39.65      A
ATOM     68  CA  LEU A   9     -21.307  24.102  37.198  1.00 39.65      A
ATOM     69  CB  LEU A   9     -20.774  25.537  37.038  1.00 33.69      A
ATOM     70  CG  LEU A   9     -19.433  25.989  37.614  1.00 33.69      A
ATOM     71  CD1 LEU A   9     -18.292  25.228  36.968  1.00 33.69      A
ATOM     72  CD2 LEU A   9     -19.275  27.487  37.387  1.00 33.69      A
ATOM     73  C   LEU A   9     -22.816  24.136  36.948  1.00 39.65      A
ATOM     74  O   LEU A   9     -23.280  23.929  35.821  1.00 39.65      A
ATOM     75  N   VAL A  10     -23.570  24.400  38.009  1.00 43.35      A
ATOM     76  CA  VAL A  10     -25.011  24.503  37.921  1.00 43.35      A
ATOM     77  CB  VAL A  10     -25.728  23.223  38.435  1.00 52.91      A
ATOM     78  CG1 VAL A  10     -25.372  22.949  39.880  1.00 52.91      A
ATOM     79  CG2 VAL A  10     -27.219  23.389  38.298  1.00 52.91      A
ATOM     80  C   VAL A  10     -25.409  25.702  38.770  1.00 43.35      A
ATOM     81  O   VAL A  10     -25.005  25.821  39.935  1.00 43.35      A
ATOM     82  N   LYS A  11     -26.191  26.595  38.175  1.00 45.06      A
ATOM     83  CA  LYS A  11     -26.634  27.794  38.862  1.00 45.06      A
ATOM     84  CB  LYS A  11     -27.457  28.667  37.913  1.00 61.94      A
ATOM     85  CG  LYS A  11     -27.732  30.067  38.450  1.00 61.94      A
ATOM     86  CD  LYS A  11     -28.623  30.840  37.503  1.00 61.94      A
ATOM     87  CE  LYS A  11     -29.030  32.183  38.076  1.00 61.94      A
ATOM     88  NZ  LYS A  11     -30.076  32.817  37.209  1.00 61.94      A
ATOM     89  C   LYS A  11     -27.444  27.494  40.119  1.00 45.06      A
ATOM     90  O   LYS A  11     -28.290  26.604  40.140  1.00 45.06      A
ATOM     91  N   ILE A  12     -27.181  28.252  41.171  1.00 38.81      A
ATOM     92  CA  ILE A  12     -27.895  28.081  42.433  1.00 38.81      A
ATOM     93  CB  ILE A  12     -26.921  28.253  43.618  1.00 40.09      A
ATOM     94  CG2 ILE A  12     -27.682  28.230  44.927  1.00 40.09      A
ATOM     95  CG1 ILE A  12     -25.846  27.160  43.563  1.00 40.09      A
ATOM     96  CD1 ILE A  12     -24.656  27.420  44.491  1.00 40.09      A
ATOM     97  C   ILE A  12     -28.986  29.157  42.509  1.00 38.81      A
ATOM     98  O   ILE A  12     -28.744  30.311  42.152  1.00 38.81      A
ATOM     99  N   ASN A  13     -30.177  28.793  42.968  1.00 47.45      A
ATOM    100  CA  ASN A  13     -31.263  29.771  43.061  1.00 47.45      A
ATOM    101  CB  ASN A  13     -32.602  29.078  43.307  1.00 60.49      A
ATOM    102  CG  ASN A  13     -33.781  30.010  43.089  1.00 60.49      A
ATOM    103  OD1 ASN A  13     -34.493  29.907  42.090  1.00 60.49      A
ATOM    104  ND2 ASN A  13     -33.981  30.938  44.014  1.00 60.49      A
ATOM    105  C   ASN A  13     -30.993  30.751  44.201  1.00 47.45      A
ATOM    106  O   ASN A  13     -30.650  30.336  45.305  1.00 47.45      A
ATOM    107  N   LYS A  14     -31.177  32.043  43.932  1.00 50.64      A
ATOM    108  CA  LYS A  14     -30.930  33.087  44.921  1.00 50.64      A
ATOM    109  CB  LYS A  14     -31.128  34.473  44.300  1.00 99.82      A
ATOM    110  CG  LYS A  14     -32.582  34.855  44.063  1.00 99.82      A
ATOM    111  CD  LYS A  14     -32.700  36.281  43.541  1.00 99.82      A
ATOM    112  CE  LYS A  14     -34.152  36.663  43.289  1.00 99.82      A
ATOM    113  NZ  LYS A  14     -34.268  38.033  42.713  1.00 99.82      A
ATOM    114  C   LYS A  14     -31.802  32.972  46.167  1.00 50.64      A
ATOM    115  O   LYS A  14     -31.497  33.563  47.201  1.00 50.64      A
ATOM    116  N   LYS A  15     -32.883  32.213  46.084  1.00 59.16      A
ATOM    117  CA  LYS A  15     -33.751  32.069  47.240  1.00 59.16      A
ATOM    118  CB  LYS A  15     -35.048  31.347  46.856  1.00 77.44      A
ATOM    119  CG  LYS A  15     -34.907  29.861  46.563  1.00 77.44      A
ATOM    120  CD  LYS A  15     -36.283  29.239  46.347  1.00 77.44      A
ATOM    121  CE  LYS A  15     -36.210  27.732  46.172  1.00 77.44      A
```

FIGURE 25 CON'T

```
ATOM    122  NZ  LYS A  15     -37.577  27.136  46.125  1.00 77.44      A
ATOM    123  C   LYS A  15     -33.042  31.316  48.365  1.00 59.16      A
ATOM    124  O   LYS A  15     -33.580  31.178  49.467  1.00 59.16      A
ATOM    125  N   ILE A  16     -31.834  30.825  48.095  1.00 58.05      A
ATOM    126  CA  ILE A  16     -31.089  30.105  49.123  1.00 58.05      A
ATOM    127  CB  ILE A  16     -30.008  29.171  48.513  1.00 56.10      A
ATOM    128  CG2 ILE A  16     -28.900  29.990  47.868  1.00 56.10      A
ATOM    129  CG1 ILE A  16     -29.429  28.281  49.614  1.00 56.10      A
ATOM    130  CD1 ILE A  16     -28.387  27.287  49.147  1.00 56.10      A
ATOM    131  C   ILE A  16     -30.413  31.101  50.062  1.00 58.05      A
ATOM    132  O   ILE A  16     -30.199  30.817  51.238  1.00 58.05      A
ATOM    133  N   ILE A  17     -30.084  32.274  49.531  1.00 60.10      A
ATOM    134  CA  ILE A  17     -29.440  33.314  50.317  1.00 60.10      A
ATOM    135  CB  ILE A  17     -29.332  34.611  49.481  1.00 48.50      A
ATOM    136  CG2 ILE A  17     -28.759  35.748  50.319  1.00 48.50      A
ATOM    137  CG1 ILE A  17     -28.445  34.335  48.256  1.00 48.50      A
ATOM    138  CD1 ILE A  17     -28.312  35.487  47.310  1.00 48.50      A
ATOM    139  C   ILE A  17     -30.251  33.522  51.600  1.00 60.10      A
ATOM    140  O   ILE A  17     -31.474  33.669  51.562  1.00 60.10      A
ATOM    141  N   PRO A  18     -29.573  33.517  52.759  1.00 61.75      A
ATOM    142  CD  PRO A  18     -28.105  33.488  52.895  1.00 41.72      A
ATOM    143  CA  PRO A  18     -30.211  33.688  54.067  1.00 61.75      A
ATOM    144  CB  PRO A  18     -29.136  33.201  55.030  1.00 41.72      A
ATOM    145  CG  PRO A  18     -27.889  33.752  54.392  1.00 41.72      A
ATOM    146  C   PRO A  18     -30.654  35.112  54.376  1.00 61.75      A
ATOM    147  O   PRO A  18     -29.958  36.074  54.055  1.00 61.75      A
ATOM    148  N   ASP A  19     -31.812  35.229  55.016  1.00101.98     A
ATOM    149  CA  ASP A  19     -32.359  36.525  55.389  1.00101.98     A
ATOM    150  CB  ASP A  19     -33.726  36.344  56.053  1.00121.69     A
ATOM    151  CG  ASP A  19     -34.729  35.656  55.146  1.00121.69     A
ATOM    152  OD1 ASP A  19     -35.052  36.221  54.080  1.00121.69     A
ATOM    153  OD2 ASP A  19     -35.191  34.549  55.498  1.00121.69     A
ATOM    154  C   ASP A  19     -31.410  37.244  56.345  1.00101.98     A
ATOM    155  O   ASP A  19     -31.004  38.379  56.088  1.00101.98     A

ATOM    156  N   LYS A  20     -31.053  36.580  57.442  1.00 78.31      A
ATOM    157  CA  LYS A  20     -30.150  37.176  58.424  1.00 78.31      A
ATOM    158  CB  LYS A  20     -30.921  37.581  59.690  1.00113.24     A
ATOM    159  CG  LYS A  20     -31.956  36.578  60.185  1.00113.24     A
ATOM    160  CD  LYS A  20     -33.246  36.672  59.382  1.00113.24     A
ATOM    161  CE  LYS A  20     -34.345  35.798  59.972  1.00113.24     A
ATOM    162  NZ  LYS A  20     -34.762  36.244  61.333  1.00113.24     A
ATOM    163  C   LYS A  20     -28.948  36.315  58.814  1.00 78.31      A
ATOM    164  O   LYS A  20     -29.064  35.109  59.018  1.00 78.31      A
ATOM    165  N   ILE A  21     -27.793  36.966  58.907  1.00 95.36      A
ATOM    166  CA  ILE A  21     -26.539  36.323  59.282  1.00 95.36      A
ATOM    167  CB  ILE A  21     -25.423  36.637  58.251  1.00 57.51      A
ATOM    168  CG2 ILE A  21     -24.108  36.017  58.699  1.00 57.51      A
ATOM    169  CG1 ILE A  21     -25.824  36.121  56.866  1.00 57.51      A
ATOM    170  CD1 ILE A  21     -24.886  36.563  55.756  1.00 57.51      A
ATOM    171  C   ILE A  21     -26.128  36.891  60.644  1.00 95.36      A
ATOM    172  O   ILE A  21     -26.275  38.087  60.890  1.00 95.36      A
ATOM    173  N   TYR A  22     -25.614  36.037  61.522  1.00 81.78      A
ATOM    174  CA  TYR A  22     -25.198  36.469  62.854  1.00 81.78      A
ATOM    175  CB  TYR A  22     -25.946  35.663  63.916  1.00 76.11      A
ATOM    176  CG  TYR A  22     -27.447  35.661  63.739  1.00 76.11      A
ATOM    177  CD1 TYR A  22     -28.228  36.741  64.161  1.00 76.11      A
```

FIGURE 25 CON'T

```
ATOM    178  CE1 TYR A  22     -29.616  36.741  63.985  1.00 76.11      A
ATOM    179  CD2 TYR A  22     -28.089  34.585  63.136  1.00 76.11      A
ATOM    180  CE2 TYR A  22     -29.469  34.575  62.955  1.00 76.11      A
ATOM    181  CZ  TYR A  22     -30.227  35.653  63.380  1.00 76.11      A
ATOM    182  OH  TYR A  22     -31.590  35.631  63.195  1.00 76.11      A
ATOM    183  C   TYR A  22     -23.694  36.297  63.054  1.00 81.78      A
ATOM    184  O   TYR A  22     -23.164  35.194  62.903  1.00 81.78      A
ATOM    185  N   VAL A  23     -23.010  37.387  63.392  1.00 68.96      A
ATOM    186  CA  VAL A  23     -21.569  37.339  63.619  1.00 68.96      A
ATOM    187  CB  VAL A  23     -20.882  38.654  63.200  1.00 64.65      A
ATOM    188  CG1 VAL A  23     -19.374  38.532  63.374  1.00 64.65      A
ATOM    189  CG2 VAL A  23     -21.217  38.983  61.755  1.00 64.65      A
ATOM    190  C   VAL A  23     -21.297  37.095  65.099  1.00 68.96      A
ATOM    191  O   VAL A  23     -21.990  37.639  65.961  1.00 68.96      A
ATOM    192  N   TYR A  24     -20.293  36.267  65.386  1.00 73.51      A
ATOM    193  CA  TYR A  24     -19.922  35.936  66.759  1.00 73.51      A
ATOM    194  CB  TYR A  24     -20.523  34.586  67.167  1.00 84.13      A
ATOM    195  CG  TYR A  24     -22.035  34.525  67.153  1.00 84.13      A
ATOM    196  CD1 TYR A  24     -22.788  35.069  68.193  1.00 84.13      A
ATOM    197  CE1 TYR A  24     -24.183  34.998  68.185  1.00 84.13      A
ATOM    198  CD2 TYR A  24     -22.713  33.911  66.101  1.00 84.13      A
ATOM    199  CE2 TYR A  24     -24.100  33.837  66.081  1.00 84.13      A
ATOM    200  CZ  TYR A  24     -24.830  34.379  67.125  1.00 84.13      A
ATOM    201  OH  TYR A  24     -26.204  34.273  67.115  1.00 84.13      A
ATOM    202  C   TYR A  24     -18.403  35.866  66.917  1.00 73.51      A
ATOM    203  O   TYR A  24     -17.672  35.607  65.956  1.00 73.51      A
ATOM    204  N   ARG A  25     -17.938  36.125  68.112  1.00 93.64      A
ATOM    205  CA  ARG A  25     -16.546  36.084  68.363  1.00 93.64      A
ATOM    206  CB  ARG A  25     -15.884  37.479  68.516  1.00 79.47      A
ATOM    207  CG  ARG A  25     -14.571  37.477  69.294  1.00 79.47      A
ATOM    208  CD  ARG A  25     -14.237  38.857  69.837  1.00 79.47      A
ATOM    209  NE  ARG A  25     -14.234  39.853  68.771  1.00 79.47      A
ATOM    210  CZ  ARG A  25     -13.304  39.964  67.829  1.00 79.47      A
ATOM    211  NH1 ARG A  25     -12.264  39.140  67.824  1.00 79.47      A
ATOM    212  NH2 ARG A  25     -13.417  40.895  66.887  1.00 79.47      A
ATOM    213  C   ARG A  25     -16.396  35.380  69.651  1.00 93.64      A
ATOM    214  O   ARG A  25     -17.187  35.516  70.592  1.00 93.64      A
ATOM    215  N   LEU A  26     -15.390  34.593  69.644  1.00100.08      A
ATOM    216  CA  LEU A  26     -14.941  33.836  70.734  1.00100.08      A
ATOM    217  CB  LEU A  26     -14.890  32.337  70.424  1.00106.38      A
ATOM    218  CG  LEU A  26     -16.199  31.672  69.939  1.00106.38      A
ATOM    219  CD1 LEU A  26     -15.940  30.278  69.378  1.00106.38      A
ATOM    220  CD2 LEU A  26     -17.209  31.596  71.075  1.00106.38      A
ATOM    221  C   LEU A  26     -13.537  34.319  71.039  1.00100.08      A
ATOM    222  O   LEU A  26     -12.996  34.050  72.115  1.00100.08      A
ATOM    223  N   TYR A  39     -14.455  18.230  68.139  1.00123.30      A
ATOM    224  CA  TYR A  39     -15.122  19.523  68.054  1.00123.30      A
ATOM    225  CB  TYR A  39     -15.739  19.886  69.404  1.00114.29      A
ATOM    226  CG  TYR A  39     -17.000  20.711  69.308  1.00114.29      A
ATOM    227  CD1 TYR A  39     -18.197  20.134  68.886  1.00114.29      A
ATOM    228  CE1 TYR A  39     -19.366  20.880  68.802  1.00114.29      A
ATOM    229  CD2 TYR A  39     -17.003  22.064  69.642  1.00114.29      A
ATOM    230  CE2 TYR A  39     -18.171  22.823  69.560  1.00114.29      A
ATOM    231  CZ  TYR A  39     -19.348  22.223  69.139  1.00114.29      A
ATOM    232  OH  TYR A  39     -20.507  22.961  69.053  1.00114.29      A
ATOM    233  C   TYR A  39     -14.105  20.589  67.663  1.00123.30      A
ATOM    234  O   TYR A  39     -12.899  20.341  67.693  1.00123.30      A
```

FIGURE 25 CON'T

```
ATOM    235  N   SER A  40     -14.594  21.772  67.303  1.00 68.80      A
ATOM    236  CA  SER A  40     -13.726  22.883  66.910  1.00 68.80      A
ATOM    237  CB  SER A  40     -12.844  22.493  65.722  1.00 73.40      A
ATOM    238  OG  SER A  40     -13.623  22.334  64.548  1.00 73.40      A
ATOM    239  C   SER A  40     -14.564  24.094  66.519  1.00 68.80      A
ATOM    240  O   SER A  40     -15.795  24.045  66.549  1.00 68.80      A
ATOM    241  N   ILE A  41     -13.885  25.176  66.149  1.00 89.34      A
ATOM    242  CA  ILE A  41     -14.556  26.407  65.747  1.00 89.34      A
ATOM    243  CB  ILE A  41     -13.568  27.590  65.691  1.00 64.37      A
ATOM    244  CG2 ILE A  41     -12.487  27.320  64.657  1.00 64.37      A
ATOM    245  CG1 ILE A  41     -14.319  28.877  65.353  1.00 64.37      A
ATOM    246  CD1 ILE A  41     -13.425  30.082  65.224  1.00 64.37      A
ATOM    247  C   ILE A  41     -15.194  26.236  64.372  1.00 89.34      A
ATOM    248  O   ILE A  41     -16.176  26.903  64.047  1.00 89.34      A
ATOM    249  N   TYR A  42     -14.621  25.342  63.570  1.00 72.02      A
ATOM    250  CA  TYR A  42     -15.133  25.058  62.235  1.00 72.02      A
ATOM    251  CB  TYR A  42     -14.070  24.330  61.408  1.00 83.35      A
ATOM    252  CG  TYR A  42     -13.024  25.237  60.793  1.00 83.35      A
ATOM    253  CD1 TYR A  42     -13.329  26.036  59.692  1.00 83.35      A
ATOM    254  CE1 TYR A  42     -12.365  26.862  59.107  1.00 83.35      A
ATOM    255  CD2 TYR A  42     -11.726  25.286  61.303  1.00 83.35      A
ATOM    256  CE2 TYR A  42     -10.753  26.107  60.727  1.00 83.35      A
ATOM    257  CZ  TYR A  42     -11.079  26.892  59.630  1.00 83.35      A
ATOM    258  OH  TYR A  42     -10.124  27.703  59.056  1.00 83.35      A
ATOM    259  C   TYR A  42     -16.383  24.196  62.357  1.00 72.02      A
ATOM    260  O   TYR A  42     -17.345  24.360  61.603  1.00 72.02      A
ATOM    261  N   ARG A  43     -16.361  23.278  63.317  1.00 72.78      A
ATOM    262  CA  ARG A  43     -17.490  22.393  63.554  1.00 72.78      A
ATOM    263  CB  ARG A  43     -17.069  21.203  64.419  1.00148.84      A
ATOM    264  CG  ARG A  43     -16.039  20.305  63.761  1.00148.84      A
ATOM    265  CD  ARG A  43     -15.670  19.134  64.650  1.00148.84      A
ATOM    266  NE  ARG A  43     -14.622  18.315  64.049  1.00148.84      A
ATOM    267  CZ  ARG A  43     -14.085  17.245  64.626  1.00148.84      A
ATOM    268  NH1 ARG A  43     -14.498  16.857  65.825  1.00148.84      A
ATOM    269  NH2 ARG A  43     -13.134  16.561  64.003  1.00148.84      A
ATOM    270  C   ARG A  43     -18.597  23.165  64.246  1.00 72.78      A
ATOM    271  O   ARG A  43     -19.780  22.869  64.060  1.00 72.78      A
ATOM    272  N   LEU A  44     -18.212  24.150  65.054  1.00 60.26      A
ATOM    273  CA  LEU A  44     -19.198  24.967  65.754  1.00 60.26      A
ATOM    274  CB  LEU A  44     -18.508  25.953  66.699  1.00 68.35      A
ATOM    275  CG  LEU A  44     -19.425  26.990  67.354  1.00 68.35      A
ATOM    276  CD1 LEU A  44     -20.435  26.291  68.256  1.00 68.35      A
ATOM    277  CD2 LEU A  44     -18.589  27.988  68.142  1.00 68.35      A
ATOM    278  C   LEU A  44     -19.981  25.729  64.695  1.00 60.26      A
ATOM    279  O   LEU A  44     -21.208  25.618  64.598  1.00 60.26      A
ATOM    280  N   ALA A  45     -19.249  26.493  63.892  1.00 60.85      A
ATOM    281  CA  ALA A  45     -19.836  27.276  62.812  1.00 60.85      A
ATOM    282  CB  ALA A  45     -18.726  27.876  61.957  1.00 58.80      A
ATOM    283  C   ALA A  45     -20.747  26.398  61.954  1.00 60.85      A

ATOM    284  O   ALA A  45     -21.842  26.812  61.576  1.00 60.85      A
ATOM    285  N   TYR A  46     -20.289  25.177  61.670  1.00 63.28      A
ATOM    286  CA  TYR A  46     -21.034  24.219  60.850  1.00 63.28      A
ATOM    287  CB  TYR A  46     -20.171  22.985  60.559  1.00 63.27      A
ATOM    288  CG  TYR A  46     -20.869  21.954  59.700  1.00 63.27      A
ATOM    289  CD1 TYR A  46     -20.767  21.998  58.308  1.00 63.27      A
ATOM    290  CE1 TYR A  46     -21.452  21.090  57.505  1.00 63.27      A
```

FIGURE 25 CON'T

```
ATOM    291  CD2 TYR A  46     -21.675  20.971  60.270  1.00 63.27      A
ATOM    292  CE2 TYR A  46     -22.370  20.060  59.475  1.00 63.27      A
ATOM    293  CZ  TYR A  46     -22.250  20.130  58.092  1.00 63.27      A
ATOM    294  OH  TYR A  46     -22.933  19.246  57.296  1.00 63.27      A
ATOM    295  C   TYR A  46     -22.341  23.748  61.476  1.00 63.28      A
ATOM    296  O   TYR A  46     -23.380  23.700  60.807  1.00 63.28      A
ATOM    297  N   GLU A  47     -22.283  23.370  62.751  1.00 72.26      A
ATOM    298  CA  GLU A  47     -23.469  22.884  63.454  1.00 72.26      A
ATOM    299  CB  GLU A  47     -23.085  22.355  64.839  1.00120.38      A
ATOM    300  CG  GLU A  47     -22.106  21.188  64.792  1.00120.38      A
ATOM    301  CD  GLU A  47     -21.873  20.556  66.151  1.00120.38      A
ATOM    302  OE1 GLU A  47     -21.515  21.287  67.097  1.00120.38      A
ATOM    303  OE2 GLU A  47     -22.043  19.324  66.271  1.00120.38      A
ATOM    304  C   GLU A  47     -24.540  23.963  63.575  1.00 72.26      A
ATOM    305  O   GLU A  47     -25.725  23.661  63.701  1.00 72.26      A
ATOM    306  N   ASN A  48     -24.120  25.222  63.524  1.00 83.72      A
ATOM    307  CA  ASN A  48     -25.059  26.333  63.611  1.00 83.72      A
ATOM    308  CB  ASN A  48     -24.462  27.458  64.467  1.00 71.59      A
ATOM    309  CG  ASN A  48     -24.410  27.102  65.950  1.00 71.59      A
ATOM    310  OD1 ASN A  48     -25.445  26.991  66.613  1.00 71.59      A
ATOM    311  ND2 ASN A  48     -23.203  26.917  66.473  1.00 71.59      A
ATOM    312  C   ASN A  48     -25.415  26.854  62.211  1.00 83.72      A
ATOM    313  O   ASN A  48     -25.897  27.975  62.058  1.00 83.72      A
ATOM    314  N   VAL A  49     -25.188  26.026  61.194  1.00 69.39      A
ATOM    315  CA  VAL A  49     -25.479  26.409  59.815  1.00 69.39      A
ATOM    316  CB  VAL A  49     -26.996  26.575  59.573  1.00 62.36      A
ATOM    317  CG1 VAL A  49     -27.275  26.655  58.075  1.00 62.36      A
ATOM    318  CG2 VAL A  49     -27.754  25.410  60.193  1.00 62.36      A
ATOM    319  C   VAL A  49     -24.791  27.734  59.520  1.00 69.39      A
ATOM    320  O   VAL A  49     -25.437  28.729  59.187  1.00 69.39      A
ATOM    321  N   GLY A  50     -23.471  27.734  59.653  1.00 52.70      A
ATOM    322  CA  GLY A  50     -22.699  28.932  59.412  1.00 52.70      A
ATOM    323  C   GLY A  50     -21.288  28.562  59.012  1.00 52.70      A
ATOM    324  O   GLY A  50     -20.981  27.379  58.832  1.00 52.70      A
ATOM    325  N   ILE A  51     -20.435  29.570  58.874  1.00 58.71      A
ATOM    326  CA  ILE A  51     -19.049  29.365  58.489  1.00 58.71      A
ATOM    327  CB  ILE A  51     -18.829  29.759  56.999  1.00 69.06      A
ATOM    328  CG2 ILE A  51     -19.485  28.727  56.089  1.00 69.06      A
ATOM    329  CG1 ILE A  51     -19.441  31.134  56.703  1.00 69.06      A
ATOM    330  CD1 ILE A  51     -18.710  32.291  57.315  1.00 69.06      A
ATOM    331  C   ILE A  51     -18.096  30.157  59.380  1.00 58.71      A
ATOM    332  O   ILE A  51     -18.528  30.830  60.322  1.00 58.71      A
ATOM    333  N   VAL A  52     -16.801  30.069  59.078  1.00 74.42      A
ATOM    334  CA  VAL A  52     -15.767  30.772  59.836  1.00 74.42      A
ATOM    335  CB  VAL A  52     -14.562  29.844  60.141  1.00 62.30      A
ATOM    336  CG1 VAL A  52     -13.472  30.618  60.874  1.00 62.30      A
ATOM    337  CG2 VAL A  52     -15.016  28.659  60.975  1.00 62.30      A
ATOM    338  C   VAL A  52     -15.266  31.967  59.030  1.00 74.42      A
ATOM    339  O   VAL A  52     -14.822  31.810  57.890  1.00 74.42      A
ATOM    340  N   ILE A  53     -15.343  33.157  59.622  1.00 97.43      A
ATOM    341  CA  ILE A  53     -14.903  34.381  58.956  1.00 97.43      A
ATOM    342  CB  ILE A  53     -15.704  35.608  59.445  1.00108.88      A
ATOM    343  CG2 ILE A  53     -15.135  36.879  58.828  1.00108.88      A
ATOM    344  CG1 ILE A  53     -17.180  35.453  59.077  1.00108.88      A
ATOM    345  CD1 ILE A  53     -18.044  36.623  59.513  1.00108.88      A
ATOM    346  C   ILE A  53     -13.421  34.668  59.177  1.00 97.43      A
ATOM    347  O   ILE A  53     -12.657  34.796  58.221  1.00 97.43      A
```

FIGURE 25 CON'T

```
ATOM    348  N   ASP A  54     -13.024  34.778  60.441  1.00 84.01      A
ATOM    349  CA  ASP A  54     -11.635  35.058  60.785  1.00 84.01      A
ATOM    350  CB  ASP A  54     -11.544  36.381  61.555  1.00 79.35      A
ATOM    351  CG  ASP A  54     -10.156  36.999  61.499  1.00 79.35      A
ATOM    352  OD1 ASP A  54      -9.165  36.277  61.745  1.00 79.35      A
ATOM    353  OD2 ASP A  54     -10.058  38.212  61.214  1.00 79.35      A
ATOM    354  C   ASP A  54     -11.079  33.917  61.641  1.00 84.01      A
ATOM    355  O   ASP A  54     -11.320  33.861  62.848  1.00 84.01      A
ATOM    356  N   PRO A  55     -10.332  32.988  61.020  1.00 99.05      A
ATOM    357  CD  PRO A  55     -10.006  32.935  59.584  1.00107.30      A
ATOM    358  CA  PRO A  55      -9.742  31.845  61.725  1.00 99.05      A
ATOM    359  CB  PRO A  55      -8.938  31.145  60.632  1.00107.30      A
ATOM    360  CG  PRO A  55      -9.698  31.474  59.387  1.00107.30      A
ATOM    361  C   PRO A  55      -8.856  32.298  62.886  1.00 99.05      A
ATOM    362  O   PRO A  55      -8.745  31.615  63.906  1.00 99.05      A
ATOM    363  N   GLU A  56      -8.225  33.455  62.715  1.00113.58      A
ATOM    364  CA  GLU A  56      -7.348  34.009  63.738  1.00113.58      A
ATOM    365  CB  GLU A  56      -6.589  35.221  63.187  1.00129.86      A
ATOM    366  CG  GLU A  56      -6.240  35.137  61.708  1.00129.86      A
ATOM    367  CD  GLU A  56      -5.482  33.875  61.350  1.00129.86      A
ATOM    368  OE1 GLU A  56      -4.412  33.630  61.946  1.00129.86      A
ATOM    369  OE2 GLU A  56      -5.958  33.128  60.469  1.00129.86      A
ATOM    370  C   GLU A  56      -8.185  34.449  64.934  1.00113.58      A
ATOM    371  O   GLU A  56      -8.154  33.829  65.997  1.00113.58      A
ATOM    372  N   ASN A  57      -8.941  35.524  64.734  1.00 99.99      A
ATOM    373  CA  ASN A  57      -9.791  36.098  65.768  1.00 99.99      A
ATOM    374  CB  ASN A  57     -10.204  37.512  65.353  1.00110.57      A
ATOM    375  CG  ASN A  57      -9.010  38.419  65.105  1.00110.57      A
ATOM    376  OD1 ASN A  57      -8.276  38.767  66.032  1.00110.57      A
ATOM    377  ND2 ASN A  57      -8.806  38.800  63.848  1.00110.57      A
ATOM    378  C   ASN A  57     -11.037  35.270  66.085  1.00 99.99      A
ATOM    379  O   ASN A  57     -11.990  35.782  66.673  1.00 99.99      A
ATOM    380  N   LEU A  58     -11.024  33.998  65.698  1.00 78.90      A
ATOM    381  CA  LEU A  58     -12.148  33.096  65.946  1.00 78.90      A
ATOM    382  CB  LEU A  58     -12.103  32.589  67.392  1.00 92.24      A
ATOM    383  CG  LEU A  58     -10.853  31.837  67.851  1.00 92.24      A
ATOM    384  CD1 LEU A  58     -10.982  31.496  69.327  1.00 92.24      A
ATOM    385  CD2 LEU A  58     -10.675  30.571  67.027  1.00 92.24      A
ATOM    386  C   LEU A  58     -13.510  33.748  65.683  1.00 78.90      A
ATOM    387  O   LEU A  58     -14.413  33.681  66.520  1.00 78.90      A
ATOM    388  N   ILE A  59     -13.654  34.375  64.520  1.00 74.85      A
ATOM    389  CA  ILE A  59     -14.907  35.034  64.159  1.00 74.85      A
ATOM    390  CB  ILE A  59     -14.642  36.384  63.466  1.00 89.43      A
ATOM    391  CG2 ILE A  59     -15.963  37.062  63.121  1.00 89.43      A
ATOM    392  CG1 ILE A  59     -13.800  37.275  64.384  1.00 89.43      A
ATOM    393  CD1 ILE A  59     -13.414  38.605  63.770  1.00 89.43      A
ATOM    394  C   ILE A  59     -15.741  34.160  63.230  1.00 74.85      A
ATOM    395  O   ILE A  59     -15.301  33.806  62.141  1.00 74.85      A
ATOM    396  N   ILE A  60     -16.945  33.812  63.671  1.00 64.45      A
ATOM    397  CA  ILE A  60     -17.840  32.978  62.879  1.00 64.45      A
ATOM    398  CB  ILE A  60     -18.218  31.689  63.639  1.00 62.85      A
ATOM    399  CG2 ILE A  60     -16.955  30.962  64.093  1.00 62.85      A
ATOM    400  CG1 ILE A  60     -19.089  32.031  64.845  1.00 62.85      A
ATOM    401  CD1 ILE A  60     -19.587  30.816  65.591  1.00 62.85      A
ATOM    402  C   ILE A  60     -19.131  33.706  62.508  1.00 64.45      A
ATOM    403  O   ILE A  60     -19.567  34.619  63.211  1.00 64.45      A
ATOM    404  N   ALA A  61     -19.732  33.289  61.397  1.00 67.87      A
```

FIGURE 25 CON'T

```
ATOM    405  CA  ALA A  61     -20.981  33.863  60.909  1.00 67.87      A
ATOM    406  CB  ALA A  61     -20.760  34.517  59.552  1.00 50.62      A
ATOM    407  C   ALA A  61     -21.990  32.723  60.799  1.00 67.87      A
ATOM    408  O   ALA A  61     -21.765  31.747  60.085  1.00 67.87      A
ATOM    409  N   THR A  62     -23.104  32.855  61.505  1.00 76.91      A
ATOM    410  CA  THR A  62     -24.134  31.824  61.536  1.00 76.91      A
ATOM    411  CB  THR A  62     -24.341  31.368  62.989  1.00 83.13      A

ATOM    412  OG1 THR A  62     -23.140  30.755  63.470  1.00 83.13      A
ATOM    413  CG2 THR A  62     -25.483  30.396  63.095  1.00 83.13      A
ATOM    414  C   THR A  62     -25.467  32.315  60.976  1.00 76.91      A
ATOM    415  O   THR A  62     -25.749  33.509  61.013  1.00 76.91      A
ATOM    416  N   THR A  63     -26.282  31.401  60.450  1.00 74.40      A
ATOM    417  CA  THR A  63     -27.588  31.788  59.922  1.00 74.40      A
ATOM    418  CB  THR A  63     -27.928  31.099  58.568  1.00 65.90      A
ATOM    419  OG1 THR A  63     -28.085  29.691  58.763  1.00 65.90      A
ATOM    420  CG2 THR A  63     -26.835  31.347  57.551  1.00 65.90      A
ATOM    421  C   THR A  63     -28.669  31.410  60.928  1.00 74.40      A
ATOM    422  O   THR A  63     -29.852  31.642  60.693  1.00 74.40      A
ATOM    423  N   LYS A  64     -28.253  30.826  62.048  1.00 78.25      A
ATOM    424  CA  LYS A  64     -29.181  30.414  63.100  1.00 78.25      A
ATOM    425  CB  LYS A  64     -29.253  28.885  63.188  1.00112.19      A
ATOM    426  CG  LYS A  64     -29.890  28.206  61.987  1.00112.19      A
ATOM    427  CD  LYS A  64     -31.329  28.658  61.789  1.00112.19      A
ATOM    428  CE  LYS A  64     -32.007  27.881  60.670  1.00112.19      A
ATOM    429  NZ  LYS A  64     -32.095  26.429  60.987  1.00112.19      A
ATOM    430  C   LYS A  64     -28.763  30.970  64.455  1.00 78.25      A
ATOM    431  O   LYS A  64     -27.661  31.492  64.608  1.00 78.25      A
ATOM    432  N   GLU A  65     -29.655  30.855  65.434  1.00 99.21      A
ATOM    433  CA  GLU A  65     -29.379  31.333  66.785  1.00 99.21      A
ATOM    434  CB  GLU A  65     -30.639  31.217  67.649  1.00164.67      A
ATOM    435  CG  GLU A  65     -30.475  31.723  69.076  1.00164.67      A
ATOM    436  CD  GLU A  65     -31.782  31.725  69.849  1.00164.67      A
ATOM    437  OE1 GLU A  65     -32.708  32.463  69.450  1.00164.67      A
ATOM    438  OE2 GLU A  65     -31.884  30.990  70.853  1.00164.67      A
ATOM    439  C   GLU A  65     -28.250  30.493  67.378  1.00 99.21      A
ATOM    440  O   GLU A  65     -28.429  29.310  67.675  1.00 99.21      A
ATOM    441  N   LEU A  66     -27.088  31.115  67.548  1.00 89.99      A
ATOM    442  CA  LEU A  66     -25.912  30.432  68.077  1.00 89.99      A
ATOM    443  CB  LEU A  66     -24.745  31.421  68.202  1.00 81.73      A
ATOM    444  CG  LEU A  66     -23.378  30.947  68.716  1.00 81.73      A
ATOM    445  CD1 LEU A  66     -23.413  30.787  70.217  1.00 81.73      A
ATOM    446  CD2 LEU A  66     -22.991  29.639  68.046  1.00 81.73      A
ATOM    447  C   LEU A  66     -26.114  29.724  69.409  1.00 89.99      A
ATOM    448  O   LEU A  66     -26.455  30.351  70.412  1.00 89.99      A
ATOM    449  N   GLU A  67     -25.902  28.411  69.406  1.00111.99      A
ATOM    450  CA  GLU A  67     -26.008  27.608  70.618  1.00111.99      A
ATOM    451  CB  GLU A  67     -26.849  26.351  70.389  1.00122.10      A
ATOM    452  CG  GLU A  67     -28.325  26.602  70.159  1.00122.10      A
ATOM    453  CD  GLU A  67     -29.129  25.316  70.173  1.00122.10      A
ATOM    454  OE1 GLU A  67     -28.814  24.407  69.374  1.00122.10      A
ATOM    455  OE2 GLU A  67     -30.073  25.212  70.984  1.00122.10      A
ATOM    456  C   GLU A  67     -24.587  27.201  70.977  1.00111.99      A
ATOM    457  O   GLU A  67     -23.938  26.464  70.236  1.00111.99      A
ATOM    458  N   TYR A  68     -24.103  27.693  72.109  1.00 96.00      A
ATOM    459  CA  TYR A  68     -22.752  27.388  72.549  1.00 96.00      A
ATOM    460  CB  TYR A  68     -21.766  28.291  71.809  1.00 74.64      A
```

FIGURE 25 CON'T

```
ATOM    461  CG  TYR A  68     -20.315  28.081  72.163  1.00 74.64      A
ATOM    462  CD1 TYR A  68     -19.759  26.800  72.202  1.00 74.64      A
ATOM    463  CE1 TYR A  68     -18.412  26.612  72.503  1.00 74.64      A
ATOM    464  CD2 TYR A  68     -19.488  29.168  72.434  1.00 74.64      A
ATOM    465  CE2 TYR A  68     -18.145  28.992  72.736  1.00 74.64      A
ATOM    466  CZ  TYR A  68     -17.612  27.716  72.769  1.00 74.64      A
ATOM    467  OH  TYR A  68     -16.278  27.556  73.068  1.00 74.64      A
ATOM    468  C   TYR A  68     -22.659  27.595  74.054  1.00 96.00      A
ATOM    469  O   TYR A  68     -22.832  28.708  74.556  1.00 96.00      A
ATOM    470  N   GLU A  69     -22.390  26.507  74.767  1.00113.97      A
ATOM    471  CA  GLU A  69     -22.289  26.532  76.218  1.00113.97      A
ATOM    472  CB  GLU A  69     -22.451  25.111  76.756  1.00132.01      A
ATOM    473  CG  GLU A  69     -23.712  24.425  76.252  1.00132.01      A
ATOM    474  CD  GLU A  69     -23.775  22.957  76.623  1.00132.01      A
ATOM    475  OE1 GLU A  69     -22.836  22.214  76.268  1.00132.01      A
ATOM    476  OE2 GLU A  69     -24.766  22.546  77.263  1.00132.01      A
ATOM    477  C   GLU A  69     -20.970  27.130  76.693  1.00113.97      A
ATOM    478  O   GLU A  69     -20.547  26.902  77.825  1.00113.97      A
ATOM    479  N   GLY A  70     -20.330  27.900  75.819  1.00103.38      A
ATOM    480  CA  GLY A  70     -19.066  28.527  76.163  1.00103.38      A
ATOM    481  C   GLY A  70     -19.118  30.039  76.041  1.00103.38      A
ATOM    482  O   GLY A  70     -20.160  30.612  75.717  1.00103.38      A
ATOM    483  N   GLU A  71     -17.989  30.691  76.301  1.00 97.46      A
ATOM    484  CA  GLU A  71     -17.910  32.144  76.220  1.00 97.46      A
ATOM    485  CB  GLU A  71     -16.650  32.646  76.933  1.00122.18      A
ATOM    486  CG  GLU A  71     -15.407  31.759  76.786  1.00122.18      A
ATOM    487  CD  GLU A  71     -15.064  31.412  75.344  1.00122.18      A
ATOM    488  OE1 GLU A  71     -15.702  30.496  74.782  1.00122.18      A
ATOM    489  OE2 GLU A  71     -14.158  32.055  74.773  1.00122.18      A
ATOM    490  C   GLU A  71     -17.920  32.650  74.782  1.00 97.46      A
ATOM    491  O   GLU A  71     -17.435  31.976  73.873  1.00 97.46      A
ATOM    492  N   PHE A  72     -18.477  33.842  74.581  1.00 79.72      A
ATOM    493  CA  PHE A  72     -18.537  34.443  73.250  1.00 79.72      A
ATOM    494  CB  PHE A  72     -19.192  33.470  72.255  1.00 65.28      A
ATOM    495  CG  PHE A  72     -20.676  33.303  72.442  1.00 65.28      A
ATOM    496  CD1 PHE A  72     -21.566  34.245  71.935  1.00 65.28      A
ATOM    497  CD2 PHE A  72     -21.183  32.196  73.115  1.00 65.28      A
ATOM    498  CE1 PHE A  72     -22.943  34.084  72.092  1.00 65.28      A
ATOM    499  CE2 PHE A  72     -22.558  32.024  73.280  1.00 65.28      A
ATOM    500  CZ  PHE A  72     -23.439  32.969  72.767  1.00 65.28      A
ATOM    501  C   PHE A  72     -19.297  35.770  73.246  1.00 79.72      A
ATOM    502  O   PHE A  72     -20.227  35.973  74.029  1.00 79.72      A
ATOM    503  N   ILE A  73     -18.895  36.670  72.357  1.00131.12      A
ATOM    504  CA  ILE A  73     -19.556  37.958  72.248  1.00131.12      A
ATOM    505  CB  ILE A  73     -18.587  39.128  72.494  1.00107.34      A
ATOM    506  CG2 ILE A  73     -17.337  38.967  71.644  1.00107.34      A
ATOM    507  CG1 ILE A  73     -19.303  40.444  72.182  1.00107.34      A
ATOM    508  CD1 ILE A  73     -18.441  41.665  72.295  1.00107.34      A
ATOM    509  C   ILE A  73     -20.168  38.133  70.865  1.00131.12      A
ATOM    510  O   ILE A  73     -19.466  38.102  69.854  1.00131.12      A
ATOM    511  N   PRO A  74     -21.494  38.312  70.803  1.00110.61      A
ATOM    512  CD  PRO A  74     -22.468  38.336  71.909  1.00106.24      A
ATOM    513  CA  PRO A  74     -22.162  38.492  69.514  1.00110.61      A
ATOM    514  CB  PRO A  74     -23.640  38.395  69.879  1.00106.24      A
ATOM    515  CG  PRO A  74     -23.672  38.979  71.260  1.00106.24      A
ATOM    516  C   PRO A  74     -21.797  39.842  68.912  1.00110.61      A
ATOM    517  O   PRO A  74     -22.059  40.884  69.510  1.00110.61      A
```

FIGURE 25 CON'T

```
ATOM    518  N   GLU A  75     -21.181  39.817  67.736  1.00 87.29      A
ATOM    519  CA  GLU A  75     -20.785  41.044  67.054  1.00 87.29      A
ATOM    520  CB  GLU A  75     -19.602  40.775  66.120  1.00 79.91      A
ATOM    521  CG  GLU A  75     -18.334  40.329  66.830  1.00 79.91      A
ATOM    522  CD  GLU A  75     -17.793  41.382  67.777  1.00 79.91      A
ATOM    523  OE1 GLU A  75     -16.732  41.139  68.391  1.00 79.91      A
ATOM    524  OE2 GLU A  75     -18.425  42.452  67.906  1.00 79.91      A
ATOM    525  C   GLU A  75     -21.952  41.616  66.257  1.00 87.29      A
ATOM    526  O   GLU A  75     -21.756  42.335  65.275  1.00 87.29      A
ATOM    527  N   GLY A  76     -23.166  41.285  66.687  1.00123.51      A
ATOM    528  CA  GLY A  76     -24.353  41.777  66.013  1.00123.51      A
ATOM    529  C   GLY A  76     -24.647  41.069  64.707  1.00123.51      A
ATOM    530  O   GLY A  76     -23.866  40.236  64.247  1.00123.51      A
ATOM    531  N   GLU A  77     -25.783  41.405  64.106  1.00 80.94      A
ATOM    532  CA  GLU A  77     -26.191  40.800  62.849  1.00 80.94      A
ATOM    533  CB  GLU A  77     -27.705  40.910  62.671  1.00 91.89      A
ATOM    534  CG  GLU A  77     -28.511  40.184  63.735  1.00 91.89      A
ATOM    535  CD  GLU A  77     -30.007  40.235  63.471  1.00 91.89      A
ATOM    536  OE1 GLU A  77     -30.777  39.706  64.303  1.00 91.89      A
ATOM    537  OE2 GLU A  77     -30.410  40.803  62.431  1.00 91.89      A
ATOM    538  C   GLU A  77     -25.492  41.462  61.679  1.00 80.94      A
ATOM    539  O   GLU A  77     -24.963  42.566  61.799  1.00 80.94      A

ATOM    540  N   ILE A  78     -25.497  40.777  60.542  1.00 71.96      A
ATOM    541  CA  ILE A  78     -24.861  41.280  59.335  1.00 71.96      A
ATOM    542  CB  ILE A  78     -23.404  40.750  59.232  1.00 94.95      A
ATOM    543  CG2 ILE A  78     -23.412  39.261  58.911  1.00 94.95      A
ATOM    544  CG1 ILE A  78     -22.630  41.506  58.153  1.00 94.95      A
ATOM    545  CD1 ILE A  78     -21.164  41.124  58.085  1.00 94.95      A
ATOM    546  C   ILE A  78     -25.678  40.788  58.142  1.00 71.96      A
ATOM    547  O   ILE A  78     -26.488  39.872  58.274  1.00 71.96      A
ATOM    548  N   SER A  79     -25.482  41.403  56.984  1.00 54.93      A
ATOM    549  CA  SER A  79     -26.202  40.985  55.794  1.00 54.93      A
ATOM    550  CB  SER A  79     -26.898  42.186  55.148  1.00 95.68      A
ATOM    551  OG  SER A  79     -25.958  43.180  54.782  1.00 95.68      A
ATOM    552  C   SER A  79     -25.247  40.330  54.793  1.00 54.93      A
ATOM    553  O   SER A  79     -24.067  40.686  54.708  1.00 54.93      A
ATOM    554  N   PHE A  80     -25.781  39.379  54.033  1.00 53.13      A
ATOM    555  CA  PHE A  80     -25.027  38.632  53.038  1.00 53.13      A
ATOM    556  CB  PHE A  80     -26.002  37.814  52.190  1.00 59.45      A
ATOM    557  CG  PHE A  80     -25.344  36.777  51.327  1.00 59.45      A
ATOM    558  CD1 PHE A  80     -24.815  35.616  51.889  1.00 59.45      A
ATOM    559  CD2 PHE A  80     -25.273  36.946  49.948  1.00 59.45      A
ATOM    560  CE1 PHE A  80     -24.231  34.637  51.086  1.00 59.45      A
ATOM    561  CE2 PHE A  80     -24.688  35.970  49.137  1.00 59.45      A
ATOM    562  CZ  PHE A  80     -24.168  34.815  49.708  1.00 59.45      A
ATOM    563  C   PHE A  80     -24.194  39.534  52.134  1.00 53.13      A
ATOM    564  O   PHE A  80     -23.107  39.153  51.686  1.00 53.13      A
ATOM    565  N   SER A  81     -24.705  40.733  51.870  1.00 50.44      A
ATOM    566  CA  SER A  81     -24.022  41.692  51.002  1.00 50.44      A
ATOM    567  CB  SER A  81     -24.933  42.895  50.733  1.00 64.56      A
ATOM    568  OG  SER A  81     -25.289  43.543  51.947  1.00 64.56      A
ATOM    569  C   SER A  81     -22.696  42.197  51.553  1.00 50.44      A
ATOM    570  O   SER A  81     -21.824  42.639  50.797  1.00 50.44      A
ATOM    571  N   GLU A  82     -22.542  42.139  52.869  1.00 66.85      A
ATOM    572  CA  GLU A  82     -21.321  42.627  53.497  1.00 66.85      A
ATOM    573  CB  GLU A  82     -21.650  43.141  54.900  1.00 83.28      A
```

FIGURE 25 CON'T

ATOM	574	CG	GLU	A	82	-22.525	44.394	54.870	1.00	83.28	A
ATOM	575	CD	GLU	A	82	-23.218	44.684	56.189	1.00	83.28	A
ATOM	576	OE1	GLU	A	82	-24.087	43.882	56.598	1.00	83.28	A
ATOM	577	OE2	GLU	A	82	-22.894	45.717	56.815	1.00	83.28	A
ATOM	578	C	GLU	A	82	-20.178	41.609	53.540	1.00	66.85	A
ATOM	579	O	GLU	A	82	-19.022	41.982	53.731	1.00	66.85	A
ATOM	580	N	LEU	A	83	-20.492	40.330	53.345	1.00	56.62	A
ATOM	581	CA	LEU	A	83	-19.459	39.300	53.358	1.00	56.62	A
ATOM	582	CB	LEU	A	83	-20.093	37.912	53.501	1.00	52.40	A
ATOM	583	CG	LEU	A	83	-20.801	37.640	54.828	1.00	52.40	A
ATOM	584	CD1	LEU	A	83	-21.641	36.383	54.724	1.00	52.40	A
ATOM	585	CD2	LEU	A	83	-19.766	37.523	55.931	1.00	52.40	A
ATOM	586	C	LEU	A	83	-18.647	39.357	52.070	1.00	56.62	A
ATOM	587	O	LEU	A	83	-19.192	39.626	50.995	1.00	56.62	A
ATOM	588	N	ARG	A	84	-17.342	39.125	52.173	1.00	53.39	A
ATOM	589	CA	ARG	A	84	-16.496	39.126	50.988	1.00	53.39	A
ATOM	590	CB	ARG	A	84	-15.017	39.007	51.380	1.00	91.29	A
ATOM	591	CG	ARG	A	84	-14.064	39.372	50.250	1.00	91.29	A
ATOM	592	CD	ARG	A	84	-12.663	39.752	50.740	1.00	91.29	A
ATOM	593	NE	ARG	A	84	-11.862	38.615	51.197	1.00	91.29	A
ATOM	594	CZ	ARG	A	84	-11.893	38.111	52.427	1.00	91.29	A
ATOM	595	NH1	ARG	A	84	-12.691	38.639	53.346	1.00	91.29	A
ATOM	596	NH2	ARG	A	84	-11.118	37.081	52.743	1.00	91.29	A
ATOM	597	C	ARG	A	84	-16.955	37.915	50.172	1.00	53.39	A
ATOM	598	O	ARG	A	84	-17.531	36.981	50.723	1.00	53.39	A
ATOM	599	N	ASN	A	85	-16.717	37.937	48.867	1.00	57.59	A
ATOM	600	CA	ASN	A	85	-17.153	36.853	47.992	1.00	57.59	A
ATOM	601	CB	ASN	A	85	-16.558	37.052	46.603	1.00	68.01	A
ATOM	602	CG	ASN	A	85	-17.033	38.333	45.957	1.00	68.01	A
ATOM	603	OD1	ASN	A	85	-18.185	38.734	46.129	1.00	68.01	A
ATOM	604	ND2	ASN	A	85	-16.155	38.979	45.202	1.00	68.01	A
ATOM	605	C	ASN	A	85	-16.853	35.443	48.495	1.00	57.59	A
ATOM	606	O	ASN	A	85	-17.744	34.586	48.536	1.00	57.59	A
ATOM	607	N	ASP	A	86	-15.600	35.217	48.875	1.00	55.76	A
ATOM	608	CA	ASP	A	86	-15.141	33.930	49.383	1.00	55.76	A
ATOM	609	CB	ASP	A	86	-13.758	34.093	50.011	1.00137.78		A
ATOM	610	CG	ASP	A	86	-12.837	34.954	49.169	1.00137.78		A
ATOM	611	OD1	ASP	A	86	-12.539	34.564	48.021	1.00137.78		A
ATOM	612	OD2	ASP	A	86	-12.415	36.025	49.655	1.00137.78		A
ATOM	613	C	ASP	A	86	-16.105	33.384	50.422	1.00	55.76	A
ATOM	614	O	ASP	A	86	-16.581	32.258	50.310	1.00	55.76	A
ATOM	615	N	TYR	A	87	-16.401	34.193	51.433	1.00	48.09	A
ATOM	616	CA	TYR	A	87	-17.301	33.773	52.502	1.00	48.09	A
ATOM	617	CB	TYR	A	87	-17.201	34.751	53.673	1.00	85.93	A
ATOM	618	CG	TYR	A	87	-15.788	34.829	54.202	1.00	85.93	A
ATOM	619	CD1	TYR	A	87	-15.143	33.686	54.677	1.00	85.93	A
ATOM	620	CE1	TYR	A	87	-13.813	33.724	55.088	1.00	85.93	A
ATOM	621	CD2	TYR	A	87	-15.068	36.021	54.162	1.00	85.93	A
ATOM	622	CE2	TYR	A	87	-13.735	36.071	54.574	1.00	85.93	A
ATOM	623	CZ	TYR	A	87	-13.115	34.917	55.033	1.00	85.93	A
ATOM	624	OH	TYR	A	87	-11.794	34.949	55.420	1.00	85.93	A
ATOM	625	C	TYR	A	87	-18.740	33.620	52.034	1.00	48.09	A
ATOM	626	O	TYR	A	87	-19.474	32.761	52.541	1.00	48.09	A
ATOM	627	N	GLN	A	88	-19.147	34.440	51.063	1.00	44.08	A
ATOM	628	CA	GLN	A	88	-20.513	34.337	50.540	1.00	44.08	A
ATOM	629	CB	GLN	A	88	-20.767	35.371	49.431	1.00	54.63	A
ATOM	630	CG	GLN	A	88	-20.763	36.823	49.883	1.00	54.63	A

FIGURE 25 CON'T

```
ATOM    631  CD  GLN A  88     -21.411  37.755  48.863  1.00 54.63      A
ATOM    632  OE1 GLN A  88     -21.115  37.694  47.674  1.00 54.63      A
ATOM    633  NE2 GLN A  88     -22.296  38.626  49.335  1.00 54.63      A
ATOM    634  C   GLN A  88     -20.681  32.928  49.966  1.00 44.08      A
ATOM    635  O   GLN A  88     -21.627  32.229  50.290  1.00 44.08      A
ATOM    636  N   SER A  89     -19.733  32.524  49.122  1.00 48.72      A
ATOM    637  CA  SER A  89     -19.754  31.209  48.494  1.00 48.72      A
ATOM    638  CB  SER A  89     -18.612  31.098  47.491  1.00 56.82      A
ATOM    639  OG  SER A  89     -18.808  31.996  46.409  1.00 56.82      A
ATOM    640  C   SER A  89     -19.658  30.090  49.528  1.00 48.72      A
ATOM    641  O   SER A  89     -20.340  29.067  49.419  1.00 48.72      A
ATOM    642  N   LYS A  90     -18.816  30.287  50.537  1.00 50.16      A
ATOM    643  CA  LYS A  90     -18.669  29.292  51.588  1.00 50.16      A
ATOM    644  CB  LYS A  90     -17.549  29.686  52.554  1.00 67.64      A
ATOM    645  CG  LYS A  90     -16.155  29.471  51.999  1.00 67.64      A
ATOM    646  CD  LYS A  90     -15.095  29.962  52.966  1.00 67.64      A
ATOM    647  CE  LYS A  90     -13.702  29.668  52.446  1.00 67.64      A
ATOM    648  NZ  LYS A  90     -12.660  30.310  53.293  1.00 67.64      A
ATOM    649  C   LYS A  90     -19.973  29.144  52.343  1.00 50.16      A
ATOM    650  O   LYS A  90     -20.401  28.027  52.641  1.00 50.16      A
ATOM    651  N   LEU A  91     -20.617  30.267  52.649  1.00 45.26      A
ATOM    652  CA  LEU A  91     -21.879  30.218  53.369  1.00 45.26      A
ATOM    653  CB  LEU A  91     -22.335  31.632  53.735  1.00 57.37      A
ATOM    654  CG  LEU A  91     -23.594  31.719  54.610  1.00 57.37      A
ATOM    655  CD1 LEU A  91     -23.430  30.848  55.854  1.00 57.37      A
ATOM    656  CD2 LEU A  91     -23.846  33.173  54.999  1.00 57.37      A
ATOM    657  C   LEU A  91     -22.950  29.506  52.533  1.00 45.26      A
ATOM    658  O   LEU A  91     -23.776  28.769  53.074  1.00 45.26      A
ATOM    659  N   VAL A  92     -22.927  29.714  51.217  1.00 42.08      A
ATOM    660  CA  VAL A  92     -23.894  29.072  50.322  1.00 42.08      A
ATOM    661  CB  VAL A  92     -23.832  29.683  48.888  1.00 46.56      A
ATOM    662  CG1 VAL A  92     -24.704  28.879  47.931  1.00 46.56      A
ATOM    663  CG2 VAL A  92     -24.298  31.134  48.921  1.00 46.56      A
ATOM    664  C   VAL A  92     -23.628  27.567  50.254  1.00 42.08      A
ATOM    665  O   VAL A  92     -24.561  26.757  50.226  1.00 42.08      A
ATOM    666  N   LEU A  93     -22.354  27.190  50.235  1.00 48.30      A
ATOM    667  CA  LEU A  93     -22.000  25.775  50.211  1.00 48.30      A

ATOM    668  CB  LEU A  93     -20.479  25.603  50.264  1.00 40.14      A
ATOM    669  CG  LEU A  93     -19.956  24.161  50.241  1.00 40.14      A
ATOM    670  CD1 LEU A  93     -20.456  23.449  48.998  1.00 40.14      A
ATOM    671  CD2 LEU A  93     -18.417  24.163  50.265  1.00 40.14      A
ATOM    672  C   LEU A  93     -22.652  25.106  51.424  1.00 48.30      A
ATOM    673  O   LEU A  93     -23.301  24.061  51.297  1.00 48.30      A
ATOM    674  N   ARG A  94     -22.493  25.718  52.598  1.00 49.80      A
ATOM    675  CA  ARG A  94     -23.095  25.183  53.822  1.00 49.80      A
ATOM    676  CB  ARG A  94     -22.714  26.037  55.036  1.00 56.97      A
ATOM    677  CG  ARG A  94     -23.425  25.620  56.318  1.00 56.97      A
ATOM    678  CD  ARG A  94     -22.934  24.260  56.798  1.00 56.97      A
ATOM    679  NE  ARG A  94     -23.634  23.785  57.990  1.00 56.97      A
ATOM    680  CZ  ARG A  94     -24.781  23.110  57.977  1.00 56.97      A
ATOM    681  NH1 ARG A  94     -25.377  22.822  56.827  1.00 56.97      A
ATOM    682  NH2 ARG A  94     -25.325  22.706  59.119  1.00 56.97      A
ATOM    683  C   ARG A  94     -24.620  25.131  53.710  1.00 49.80      A
ATOM    684  O   ARG A  94     -25.248  24.167  54.155  1.00 49.80      A
ATOM    685  N   LEU A  95     -25.217  26.166  53.119  1.00 58.97      A
ATOM    686  CA  LEU A  95     -26.672  26.204  52.958  1.00 58.97      A
```

FIGURE 25 CON'T

```
ATOM    687  CB  LEU A  95     -27.128  27.587  52.468  1.00 59.80      A
ATOM    688  CG  LEU A  95     -27.061  28.699  53.525  1.00 59.80      A
ATOM    689  CD1 LEU A  95     -27.396  30.043  52.905  1.00 59.80      A
ATOM    690  CD2 LEU A  95     -28.026  28.375  54.661  1.00 59.80      A
ATOM    691  C   LEU A  95     -27.161  25.116  52.005  1.00 58.97      A
ATOM    692  O   LEU A  95     -28.223  24.530  52.218  1.00 58.97      A
ATOM    693  N   LEU A  96     -26.398  24.848  50.947  1.00 52.25      A
ATOM    694  CA  LEU A  96     -26.777  23.788  50.012  1.00 52.25      A
ATOM    695  CB  LEU A  96     -25.732  23.649  48.893  1.00 39.29      A
ATOM    696  CG  LEU A  96     -25.807  24.714  47.790  1.00 39.29      A
ATOM    697  CD1 LEU A  96     -24.683  24.540  46.806  1.00 39.29      A
ATOM    698  CD2 LEU A  96     -27.155  24.593  47.086  1.00 39.29      A
ATOM    699  C   LEU A  96     -26.894  22.465  50.772  1.00 52.25      A
ATOM    700  O   LEU A  96     -27.829  21.690  50.556  1.00 52.25      A
ATOM    701  N   LYS A  97     -25.942  22.219  51.667  1.00 61.38      A
ATOM    702  CA  LYS A  97     -25.927  20.994  52.462  1.00 61.38      A
ATOM    703  CB  LYS A  97     -24.729  20.994  53.412  1.00 64.44      A
ATOM    704  CG  LYS A  97     -24.551  19.703  54.207  1.00 64.44      A
ATOM    705  CD  LYS A  97     -23.899  18.619  53.361  1.00 64.44      A
ATOM    706  CE  LYS A  97     -23.566  17.382  54.184  1.00 64.44      A
ATOM    707  NZ  LYS A  97     -24.768  16.670  54.680  1.00 64.44      A
ATOM    708  C   LYS A  97     -27.211  20.852  53.275  1.00 61.38      A
ATOM    709  O   LYS A  97     -27.734  19.747  53.434  1.00 61.38      A
ATOM    710  N   GLU A  98     -27.720  21.968  53.791  1.00 62.33      A
ATOM    711  CA  GLU A  98     -28.944  21.932  54.584  1.00 62.33      A
ATOM    712  CB  GLU A  98     -29.188  23.278  55.271  1.00 83.72      A
ATOM    713  CG  GLU A  98     -28.308  23.498  56.484  1.00 83.72      A
ATOM    714  CD  GLU A  98     -28.430  22.368  57.498  1.00 83.72      A
ATOM    715  OE1 GLU A  98     -29.536  22.178  58.048  1.00 83.72      A
ATOM    716  OE2 GLU A  98     -27.422  21.667  57.740  1.00 83.72      A
ATOM    717  C   GLU A  98     -30.163  21.539  53.767  1.00 62.33      A
ATOM    718  O   GLU A  98     -31.200  21.186  54.327  1.00 62.33      A
ATOM    719  N   ASN A  99     -30.043  21.599  52.445  1.00 61.59      A
ATOM    720  CA  ASN A  99     -31.153  21.224  51.589  1.00 61.59      A
ATOM    721  CB  ASN A  99     -31.361  22.255  50.480  1.00 72.80      A
ATOM    722  CG  ASN A  99     -31.899  23.573  51.007  1.00 72.80      A
ATOM    723  OD1 ASN A  99     -31.174  24.347  51.636  1.00 72.80      A
ATOM    724  ND2 ASN A  99     -33.182  23.826  50.765  1.00 72.80      A
ATOM    725  C   ASN A  99     -30.902  19.857  50.983  1.00 61.59      A
ATOM    726  O   ASN A  99     -31.506  19.500  49.972  1.00 61.59      A
ATOM    727  N   GLY A 100     -30.002  19.100  51.607  1.00 63.74      A
ATOM    728  CA  GLY A 100     -29.684  17.768  51.126  1.00 63.74      A
ATOM    729  C   GLY A 100     -28.749  17.717  49.932  1.00 63.74      A
ATOM    730  O   GLY A 100     -28.641  16.687  49.269  1.00 63.74      A
ATOM    731  N   ILE A 101     -28.071  18.821  49.642  1.00 49.44      A
ATOM    732  CA  ILE A 101     -27.148  18.844  48.515  1.00 49.44      A
ATOM    733  CB  ILE A 101     -27.453  20.023  47.575  1.00 51.42      A
ATOM    734  CG2 ILE A 101     -26.437  20.066  46.432  1.00 51.42      A
ATOM    735  CG1 ILE A 101     -28.873  19.871  47.022  1.00 51.42      A
ATOM    736  CD1 ILE A 101     -29.328  21.045  46.203  1.00 51.42      A
ATOM    737  C   ILE A 101     -25.722  18.951  49.035  1.00 49.44      A
ATOM    738  O   ILE A 101     -25.212  20.049  49.255  1.00 49.44      A
ATOM    739  N   GLY A 102     -25.097  17.795  49.245  1.00 43.56      A
ATOM    740  CA  GLY A 102     -23.734  17.758  49.744  1.00 43.56      A
ATOM    741  C   GLY A 102     -22.955  16.629  49.100  1.00 43.56      A
ATOM    742  O   GLY A 102     -23.513  15.823  48.349  1.00 43.56      A
ATOM    743  N   GLU A 103     -21.665  16.560  49.391  1.00 42.81      A
```

FIGURE 25 CON'T

```
ATOM    744  CA  GLU A 103     -20.827  15.517  48.819  1.00 42.81      A
ATOM    745  CB  GLU A 103     -19.385  15.702  49.282  1.00 48.36      A
ATOM    746  CG  GLU A 103     -18.764  16.951  48.688  1.00 48.36      A
ATOM    747  CD  GLU A 103     -17.347  17.165  49.132  1.00 48.36      A
ATOM    748  OE1 GLU A 103     -16.671  18.048  48.569  1.00 48.36      A
ATOM    749  OE2 GLU A 103     -16.905  16.451  50.050  1.00 48.36      A
ATOM    750  C   GLU A 103     -21.321  14.123  49.161  1.00 42.81      A
ATOM    751  O   GLU A 103     -21.320  13.234  48.311  1.00 42.81      A
ATOM    752  N   TYR A 104     -21.751  13.935  50.404  1.00 45.75      A
ATOM    753  CA  TYR A 104     -22.253  12.642  50.838  1.00 45.75      A
ATOM    754  CB  TYR A 104     -22.697  12.707  52.300  1.00 64.47      A
ATOM    755  CG  TYR A 104     -23.400  11.453  52.767  1.00 64.47      A
ATOM    756  CD1 TYR A 104     -22.714  10.245  52.870  1.00 64.47      A
ATOM    757  CE1 TYR A 104     -23.357   9.083  53.292  1.00 64.47      A
ATOM    758  CD2 TYR A 104     -24.754  11.472  53.097  1.00 64.47      A
ATOM    759  CE2 TYR A 104     -25.409  10.317  53.522  1.00 64.47      A
ATOM    760  CZ  TYR A 104     -24.704   9.124  53.618  1.00 64.47      A
ATOM    761  OH  TYR A 104     -25.341   7.977  54.049  1.00 64.47      A
ATOM    762  C   TYR A 104     -23.431  12.202  49.972  1.00 45.75      A
ATOM    763  O   TYR A 104     -23.380  11.156  49.327  1.00 45.75      A
ATOM    764  N   GLU A 105     -24.490  13.007  49.955  1.00 43.71      A
ATOM    765  CA  GLU A 105     -25.683  12.683  49.172  1.00 43.71      A
ATOM    766  CB  GLU A 105     -26.764  13.751  49.376  1.00 62.74      A
ATOM    767  CG  GLU A 105     -27.287  13.911  50.803  1.00 62.74      A
ATOM    768  CD  GLU A 105     -26.311  14.619  51.723  1.00 62.74      A
ATOM    769  OE1 GLU A 105     -25.458  15.386  51.225  1.00 62.74      A
ATOM    770  OE2 GLU A 105     -26.407  14.421  52.952  1.00 62.74      A
ATOM    771  C   GLU A 105     -25.431  12.526  47.662  1.00 43.71      A
ATOM    772  O   GLU A 105     -25.856  11.544  47.064  1.00 43.71      A
ATOM    773  N   LEU A 106     -24.754  13.490  47.040  1.00 39.82      A
ATOM    774  CA  LEU A 106     -24.504  13.402  45.606  1.00 39.82      A
ATOM    775  CB  LEU A 106     -24.109  14.779  45.042  1.00 40.67      A
ATOM    776  CG  LEU A 106     -25.330  15.671  44.722  1.00 40.67      A
ATOM    777  CD1 LEU A 106     -26.094  16.030  45.998  1.00 40.67      A
ATOM    778  CD2 LEU A 106     -24.872  16.930  44.023  1.00 40.67      A
ATOM    779  C   LEU A 106     -23.489  12.325  45.204  1.00 39.82      A
ATOM    780  O   LEU A 106     -23.542  11.822  44.082  1.00 39.82      A
ATOM    781  N   SER A 107     -22.570  11.966  46.103  1.00 38.34      A
ATOM    782  CA  SER A 107     -21.611  10.905  45.794  1.00 38.34      A
ATOM    783  CB  SER A 107     -20.526  10.800  46.870  1.00 39.34      A
ATOM    784  OG  SER A 107     -19.582  11.852  46.752  1.00 39.34      A
ATOM    785  C   SER A 107     -22.385   9.589  45.706  1.00 38.34      A
ATOM    786  O   SER A 107     -22.087   8.730  44.872  1.00 38.34      A
ATOM    787  N   LYS A 108     -23.388   9.436  46.568  1.00 46.95      A
ATOM    788  CA  LYS A 108     -24.212   8.231  46.549  1.00 46.95      A
ATOM    789  CB  LYS A 108     -25.175   8.218  47.740  1.00 70.68      A
ATOM    790  CG  LYS A 108     -24.480   7.977  49.075  1.00 70.68      A
ATOM    791  CD  LYS A 108     -25.396   8.254  50.258  1.00 70.68      A
ATOM    792  CE  LYS A 108     -26.610   7.350  50.247  1.00 70.68      A
ATOM    793  NZ  LYS A 108     -27.445   7.570  51.455  1.00 70.68      A
ATOM    794  C   LYS A 108     -24.990   8.184  45.235  1.00 46.95      A
ATOM    795  O   LYS A 108     -25.078   7.141  44.600  1.00 46.95      A

ATOM    796  N   LEU A 109     -25.549   9.319  44.825  1.00 42.18      A
ATOM    797  CA  LEU A 109     -26.291   9.376  43.575  1.00 42.18      A
ATOM    798  CB  LEU A 109     -26.873  10.783  43.358  1.00 40.49      A
ATOM    799  CG  LEU A 109     -27.945  11.260  44.354  1.00 40.49      A
```

FIGURE 25 CON'T

```
ATOM    800  CD1 LEU A 109     -28.387  12.689  44.012  1.00 40.49      A
ATOM    801  CD2 LEU A 109     -29.150  10.316  44.331  1.00 40.49      A
ATOM    802  C   LEU A 109     -25.373   8.983  42.410  1.00 42.18      A
ATOM    803  O   LEU A 109     -25.772   8.217  41.539  1.00 42.18      A
ATOM    804  N   LEU A 110     -24.146   9.499  42.395  1.00 37.22      A
ATOM    805  CA  LEU A 110     -23.194   9.163  41.329  1.00 37.22      A
ATOM    806  CB  LEU A 110     -21.843   9.869  41.557  1.00 28.86      A
ATOM    807  CG  LEU A 110     -20.639   9.415  40.701  1.00 28.86      A
ATOM    808  CD1 LEU A 110     -20.876   9.791  39.218  1.00 28.86      A
ATOM    809  CD2 LEU A 110     -19.329  10.081  41.214  1.00 28.86      A
ATOM    810  C   LEU A 110     -22.943   7.658  41.215  1.00 37.22      A
ATOM    811  O   LEU A 110     -22.899   7.101  40.101  1.00 37.22      A
ATOM    812  N   ARG A 111     -22.761   7.001  42.356  1.00 45.48      A
ATOM    813  CA  ARG A 111     -22.495   5.569  42.353  1.00 45.48      A
ATOM    814  CB  ARG A 111     -21.988   5.111  43.730  1.00 39.33      A
ATOM    815  CG  ARG A 111     -20.594   5.692  44.031  1.00 39.33      A
ATOM    816  CD  ARG A 111     -19.960   5.096  45.270  1.00 39.33      A
ATOM    817  NE  ARG A 111     -20.584   5.586  46.496  1.00 39.33      A
ATOM    818  CZ  ARG A 111     -20.157   6.633  47.196  1.00 39.33      A
ATOM    819  NH1 ARG A 111     -19.089   7.316  46.794  1.00 39.33      A
ATOM    820  NH2 ARG A 111     -20.799   6.990  48.305  1.00 39.33      A
ATOM    821  C   ARG A 111     -23.685   4.737  41.891  1.00 45.48      A
ATOM    822  O   ARG A 111     -23.585   3.516  41.753  1.00 45.48      A
ATOM    823  N   LYS A 112     -24.808   5.397  41.629  1.00 49.69      A
ATOM    824  CA  LYS A 112     -25.963   4.676  41.122  1.00 49.69      A
ATOM    825  CB  LYS A 112     -27.249   5.481  41.321  1.00 66.26      A
ATOM    826  CG  LYS A 112     -27.793   5.461  42.733  1.00 66.26      A
ATOM    827  CD  LYS A 112     -29.187   6.068  42.771  1.00 66.26      A
ATOM    828  CE  LYS A 112     -29.856   5.845  44.120  1.00 66.26      A
ATOM    829  NZ  LYS A 112     -31.276   6.297  44.113  1.00 66.26      A
ATOM    830  C   LYS A 112     -25.729   4.455  39.629  1.00 49.69      A
ATOM    831  O   LYS A 112     -26.286   3.531  39.032  1.00 49.69      A
ATOM    832  N   PHE A 113     -24.881   5.301  39.045  1.00 44.64      A
ATOM    833  CA  PHE A 113     -24.569   5.248  37.614  1.00 44.64      A
ATOM    834  CB  PHE A 113     -24.845   6.617  36.996  1.00 42.87      A
ATOM    835  CG  PHE A 113     -26.215   7.152  37.323  1.00 42.87      A
ATOM    836  CD1 PHE A 113     -27.331   6.729  36.607  1.00 42.87      A
ATOM    837  CD2 PHE A 113     -26.397   8.034  38.386  1.00 42.87      A
ATOM    838  CE1 PHE A 113     -28.608   7.171  36.948  1.00 42.87      A
ATOM    839  CE2 PHE A 113     -27.675   8.483  38.735  1.00 42.87      A
ATOM    840  CZ  PHE A 113     -28.782   8.047  38.014  1.00 42.87      A
ATOM    841  C   PHE A 113     -23.133   4.827  37.313  1.00 44.64      A
ATOM    842  O   PHE A 113     -22.881   4.157  36.309  1.00 44.64      A
ATOM    843  N   ARG A 114     -22.198   5.243  38.169  1.00 42.32      A
ATOM    844  CA  ARG A 114     -20.784   4.899  38.022  1.00 42.32      A
ATOM    845  CB  ARG A 114     -19.933   6.167  37.868  1.00 50.54      A
ATOM    846  CG  ARG A 114     -18.470   5.926  37.474  1.00 50.54      A
ATOM    847  CD  ARG A 114     -18.357   5.175  36.149  1.00 50.54      A
ATOM    848  NE  ARG A 114     -17.008   5.231  35.590  1.00 50.54      A
ATOM    849  CZ  ARG A 114     -16.596   4.539  34.529  1.00 50.54      A
ATOM    850  NH1 ARG A 114     -17.430   3.723  33.896  1.00 50.54      A
ATOM    851  NH2 ARG A 114     -15.344   4.648  34.106  1.00 50.54      A
ATOM    852  C   ARG A 114     -20.428   4.167  39.316  1.00 42.32      A
ATOM    853  O   ARG A 114     -20.106   4.785  40.339  1.00 42.32      A
ATOM    854  N   LYS A 115     -20.496   2.844  39.260  1.00 44.60      A
ATOM    855  CA  LYS A 115     -20.248   2.008  40.433  1.00 44.60      A
ATOM    856  CB  LYS A 115     -20.946   0.657  40.255  1.00 77.56      A
```

FIGURE 25 CON'T

```
ATOM    857  CG  LYS A 115     -22.445   0.743  40.062  1.00 77.56      A
ATOM    858  CD  LYS A 115     -23.035  -0.639  39.853  1.00 77.56      A
ATOM    859  CE  LYS A 115     -24.543  -0.582  39.674  1.00 77.56      A
ATOM    860  NZ  LYS A 115     -25.133  -1.952  39.542  1.00 77.56      A
ATOM    861  C   LYS A 115     -18.795   1.747  40.795  1.00 44.60      A
ATOM    862  O   LYS A 115     -17.912   1.822  39.954  1.00 44.60      A
ATOM    863  N   PRO A 116     -18.534   1.449  42.076  1.00 45.82      A
ATOM    864  CD  PRO A 116     -19.441   1.560  43.227  1.00 41.36      A
ATOM    865  CA  PRO A 116     -17.172   1.161  42.521  1.00 45.82      A
ATOM    866  CB  PRO A 116     -17.343   0.883  44.013  1.00 41.36      A
ATOM    867  CG  PRO A 116     -18.457   1.773  44.387  1.00 41.36      A
ATOM    868  C   PRO A 116     -16.751  -0.094  41.772  1.00 45.82      A
ATOM    869  O   PRO A 116     -17.578  -0.970  41.504  1.00 45.82      A
ATOM    870  N   LYS A 117     -15.474  -0.194  41.442  1.00 44.22      A
ATOM    871  CA  LYS A 117     -15.002  -1.361  40.724  1.00 44.22      A
ATOM    872  CB  LYS A 117     -14.766  -1.003  39.258  1.00 53.13      A
ATOM    873  CG  LYS A 117     -14.467  -2.185  38.357  1.00 53.13      A
ATOM    874  CD  LYS A 117     -14.588  -1.775  36.896  1.00 53.13      A
ATOM    875  CE  LYS A 117     -14.312  -2.934  35.946  1.00 53.13      A
ATOM    876  NZ  LYS A 117     -14.623  -2.553  34.526  1.00 53.13      A
ATOM    877  C   LYS A 117     -13.712  -1.820  41.380  1.00 44.22      A
ATOM    878  O   LYS A 117     -12.877  -1.004  41.766  1.00 44.22      A
ATOM    879  N   THR A 118     -13.553  -3.131  41.509  1.00 52.99      A
ATOM    880  CA  THR A 118     -12.363  -3.672  42.135  1.00 52.99      A
ATOM    881  CB  THR A 118     -12.730  -4.747  43.168  1.00 74.27      A
ATOM    882  OG1 THR A 118     -13.546  -5.744  42.546  1.00 74.27      A
ATOM    883  CG2 THR A 118     -13.496  -4.128  44.325  1.00 74.27      A
ATOM    884  C   THR A 118     -11.394  -4.260  41.130  1.00 52.99      A
ATOM    885  O   THR A 118     -11.786  -4.960  40.201  1.00 52.99      A
ATOM    886  N   PHE A 119     -10.123  -3.941  41.319  1.00 43.70      A
ATOM    887  CA  PHE A 119      -9.043  -4.434  40.469  1.00 43.70      A
ATOM    888  CB  PHE A 119      -8.372  -3.274  39.714  1.00 50.21      A
ATOM    889  CG  PHE A 119      -9.294  -2.541  38.763  1.00 50.21      A
ATOM    890  CD1 PHE A 119      -9.266  -2.811  37.393  1.00 50.21      A
ATOM    891  CD2 PHE A 119     -10.199  -1.597  39.239  1.00 50.21      A
ATOM    892  CE1 PHE A 119     -10.137  -2.142  36.508  1.00 50.21      A
ATOM    893  CE2 PHE A 119     -11.067  -0.931  38.371  1.00 50.21      A
ATOM    894  CZ  PHE A 119     -11.037  -1.202  37.003  1.00 50.21      A
ATOM    895  C   PHE A 119      -8.055  -5.046  41.454  1.00 43.70      A
ATOM    896  O   PHE A 119      -7.467  -4.328  42.280  1.00 43.70      A
ATOM    897  N   GLY A 120      -7.883  -6.364  41.393  1.00 44.94      A
ATOM    898  CA  GLY A 120      -6.966  -7.019  42.312  1.00 44.94      A
ATOM    899  C   GLY A 120      -7.471  -6.796  43.723  1.00 44.94      A
ATOM    900  O   GLY A 120      -8.652  -7.033  44.002  1.00 44.94      A
ATOM    901  N   ASP A 121      -6.598  -6.326  44.610  1.00 55.66      A
ATOM    902  CA  ASP A 121      -6.980  -6.071  45.999  1.00 55.66      A
ATOM    903  CB  ASP A 121      -5.795  -6.302  46.950  1.00 64.03      A
ATOM    904  CG  ASP A 121      -5.403  -7.762  47.070  1.00 64.03      A
ATOM    905  OD1 ASP A 121      -6.305  -8.622  47.160  1.00 64.03      A
ATOM    906  OD2 ASP A 121      -4.186  -8.043  47.095  1.00 64.03      A
ATOM    907  C   ASP A 121      -7.467  -4.643  46.214  1.00 55.66      A
ATOM    908  O   ASP A 121      -7.723  -4.242  47.350  1.00 55.66      A
ATOM    909  N   TYR A 122      -7.598  -3.874  45.140  1.00 49.08      A
ATOM    910  CA  TYR A 122      -8.014  -2.485  45.276  1.00 49.08      A
ATOM    911  CB  TYR A 122      -6.972  -1.577  44.618  1.00 51.10      A
ATOM    912  CG  TYR A 122      -5.632  -1.582  45.312  1.00 51.10      A
ATOM    913  CD1 TYR A 122      -5.347  -0.674  46.343  1.00 51.10      A
```

FIGURE 25 CON'T

```
ATOM    914  CE1 TYR A 122      -4.136  -0.713  47.018  1.00 51.10      A
ATOM    915  CD2 TYR A 122      -4.665  -2.526  44.977  1.00 51.10      A
ATOM    916  CE2 TYR A 122      -3.443  -2.577  45.648  1.00 51.10      A
ATOM    917  CZ  TYR A 122      -3.186  -1.672  46.666  1.00 51.10      A
ATOM    918  OH  TYR A 122      -1.991  -1.748  47.334  1.00 51.10      A
ATOM    919  C   TYR A 122      -9.396  -2.162  44.713  1.00 49.08      A
ATOM    920  O   TYR A 122      -9.815  -2.703  43.694  1.00 49.08      A
ATOM    921  N   LYS A 123     -10.110  -1.276  45.389  1.00 46.45      A
ATOM    922  CA  LYS A 123     -11.421  -0.875  44.912  1.00 46.45      A
ATOM    923  CB  LYS A 123     -12.487  -1.060  45.995  1.00 59.84      A

ATOM    924  CG  LYS A 123     -13.869  -0.625  45.526  1.00 59.84      A
ATOM    925  CD  LYS A 123     -14.896  -0.609  46.648  1.00 59.84      A
ATOM    926  CE  LYS A 123     -15.216  -2.012  47.147  1.00 59.84      A
ATOM    927  NZ  LYS A 123     -16.267  -1.971  48.202  1.00 59.84      A
ATOM    928  C   LYS A 123     -11.369   0.597  44.518  1.00 46.45      A
ATOM    929  O   LYS A 123     -10.870   1.423  45.281  1.00 46.45      A
ATOM    930  N   VAL A 124     -11.858   0.910  43.322  1.00 43.32      A
ATOM    931  CA  VAL A 124     -11.918   2.288  42.843  1.00 43.32      A
ATOM    932  CB  VAL A 124     -11.800   2.382  41.313  1.00 44.39      A
ATOM    933  CG1 VAL A 124     -11.982   3.837  40.884  1.00 44.39      A
ATOM    934  CG2 VAL A 124     -10.447   1.857  40.856  1.00 44.39      A
ATOM    935  C   VAL A 124     -13.290   2.823  43.242  1.00 43.32      A
ATOM    936  O   VAL A 124     -14.317   2.299  42.812  1.00 43.32      A
ATOM    937  N   ILE A 125     -13.306   3.874  44.051  1.00 34.73      A
ATOM    938  CA  ILE A 125     -14.553   4.436  44.530  1.00 34.73      A
ATOM    939  CB  ILE A 125     -14.541   4.499  46.075  1.00 39.71      A
ATOM    940  CG2 ILE A 125     -15.887   4.976  46.592  1.00 39.71      A
ATOM    941  CG1 ILE A 125     -14.182   3.123  46.639  1.00 39.71      A
ATOM    942  CD1 ILE A 125     -14.110   3.068  48.154  1.00 39.71      A
ATOM    943  C   ILE A 125     -14.856   5.829  43.986  1.00 34.73      A
ATOM    944  O   ILE A 125     -14.173   6.798  44.327  1.00 34.73      A
ATOM    945  N   PRO A 126     -15.877   5.949  43.122  1.00 42.89      A
ATOM    946  CD  PRO A 126     -16.561   4.868  42.383  1.00 37.78      A
ATOM    947  CA  PRO A 126     -16.225   7.269  42.572  1.00 42.89      A
ATOM    948  CB  PRO A 126     -17.132   6.942  41.375  1.00 37.78      A
ATOM    949  CG  PRO A 126     -16.767   5.492  41.020  1.00 37.78      A
ATOM    950  C   PRO A 126     -16.993   8.071  43.608  1.00 42.89      A
ATOM    951  O   PRO A 126     -17.765   7.508  44.396  1.00 42.89      A
ATOM    952  N   SER A 127     -16.782   9.385  43.611  1.00 41.13      A
ATOM    953  CA  SER A 127     -17.506  10.268  44.519  1.00 41.13      A
ATOM    954  CB  SER A 127     -16.859  10.272  45.912  1.00 36.83      A
ATOM    955  OG  SER A 127     -15.702  11.086  45.931  1.00 36.83      A
ATOM    956  C   SER A 127     -17.448  11.664  43.898  1.00 41.13      A
ATOM    957  O   SER A 127     -16.843  11.848  42.842  1.00 41.13      A
ATOM    958  N   VAL A 128     -18.088  12.642  44.524  1.00 41.04      A
ATOM    959  CA  VAL A 128     -18.025  13.989  43.985  1.00 41.04      A
ATOM    960  CB  VAL A 128     -19.399  14.532  43.538  1.00 42.52      A
ATOM    961  CG1 VAL A 128     -19.995  13.633  42.454  1.00 42.52      A
ATOM    962  CG2 VAL A 128     -20.325  14.647  44.736  1.00 42.52      A
ATOM    963  C   VAL A 128     -17.459  14.980  44.978  1.00 41.04      A
ATOM    964  O   VAL A 128     -17.731  14.923  46.175  1.00 41.04      A
ATOM    965  N   GLU A 129     -16.672  15.898  44.445  1.00 39.23      A
ATOM    966  CA  GLU A 129     -16.056  16.966  45.209  1.00 39.23      A
ATOM    967  CB  GLU A 129     -14.622  17.111  44.716  1.00 59.10      A
ATOM    968  CG  GLU A 129     -13.759  18.136  45.388  1.00 59.10      A
ATOM    969  CD  GLU A 129     -12.330  18.002  44.909  1.00 59.10      A
```

FIGURE 25 CON'T

```
ATOM    970  OE1 GLU A 129     -11.606  17.123  45.422  1.00 59.10      A
ATOM    971  OE2 GLU A 129     -11.938  18.748  43.997  1.00 59.10      A
ATOM    972  C   GLU A 129     -16.909  18.200  44.858  1.00 39.23      A
ATOM    973  O   GLU A 129     -17.144  18.476  43.681  1.00 39.23      A
ATOM    974  N   MSE A 130     -17.379  18.932  45.864  1.00 46.88      A
ATOM    975  CA  MSE A 130     -18.217  20.100  45.594  1.00 46.88      A
ATOM    976  CB  MSE A 130     -19.645  19.832  46.076  1.00 52.07      A
ATOM    977  CG  MSE A 130     -20.450  18.959  45.129  1.00 52.07      A
ATOM    978  SE  MSE A 130     -21.832  17.956  46.025  1.00 52.07      A
ATOM    979  CE  MSE A 130     -22.671  19.372  47.043  1.00 52.07      A
ATOM    980  C   MSE A 130     -17.739  21.425  46.177  1.00 46.88      A
ATOM    981  O   MSE A 130     -17.205  21.477  47.287  1.00 46.88      A
ATOM    982  N   SER A 131     -17.954  22.498  45.416  1.00 38.88      A
ATOM    983  CA  SER A 131     -17.580  23.840  45.846  1.00 38.88      A
ATOM    984  CB  SER A 131     -16.118  24.140  45.483  1.00 37.16      A
ATOM    985  OG  SER A 131     -15.933  24.200  44.082  1.00 37.16      A
ATOM    986  C   SER A 131     -18.517  24.863  45.197  1.00 38.88      A
ATOM    987  O   SER A 131     -19.308  24.529  44.316  1.00 38.88      A
ATOM    988  N   VAL A 132     -18.436  26.106  45.653  1.00 43.58      A
ATOM    989  CA  VAL A 132     -19.269  27.175  45.130  1.00 43.58      A
ATOM    990  CB  VAL A 132     -20.210  27.731  46.211  1.00 43.96      A
ATOM    991  CG1 VAL A 132     -20.951  28.969  45.685  1.00 43.96      A
ATOM    992  CG2 VAL A 132     -21.188  26.656  46.643  1.00 43.96      A
ATOM    993  C   VAL A 132     -18.406  28.312  44.610  1.00 43.58      A
ATOM    994  O   VAL A 132     -17.508  28.802  45.307  1.00 43.58      A
ATOM    995  N   ILE A 133     -18.683  28.717  43.373  1.00 43.62      A
ATOM    996  CA  ILE A 133     -17.968  29.807  42.732  1.00 43.62      A
ATOM    997  CB  ILE A 133     -17.324  29.349  41.409  1.00 42.01      A
ATOM    998  CG2 ILE A 133     -16.682  30.540  40.710  1.00 42.01      A
ATOM    999  CG1 ILE A 133     -16.247  28.290  41.673  1.00 42.01      A
ATOM   1000  CD1 ILE A 133     -15.498  27.875  40.405  1.00 42.01      A
ATOM   1001  C   ILE A 133     -18.945  30.955  42.427  1.00 43.62      A
ATOM   1002  O   ILE A 133     -20.065  30.730  41.945  1.00 43.62      A
ATOM   1003  N   LYS A 134     -18.538  32.182  42.730  1.00 47.61      A
ATOM   1004  CA  LYS A 134     -19.389  33.328  42.429  1.00 47.61      A
ATOM   1005  CB  LYS A 134     -19.263  34.412  43.504  1.00 46.47      A
ATOM   1006  CG  LYS A 134     -20.306  35.536  43.371  1.00 46.47      A
ATOM   1007  CD  LYS A 134     -19.960  36.727  44.246  1.00 46.47      A
ATOM   1008  CE  LYS A 134     -21.094  37.759  44.307  1.00 46.47      A
ATOM   1009  NZ  LYS A 134     -20.755  38.892  45.219  1.00 46.47      A
ATOM   1010  C   LYS A 134     -18.875  33.864  41.097  1.00 47.61      A
ATOM   1011  O   LYS A 134     -17.729  34.306  41.013  1.00 47.61      A
ATOM   1012  N   HIS A 135     -19.677  33.791  40.040  1.00 73.70      A
ATOM   1013  CA  HIS A 135     -19.179  34.309  38.781  1.00 73.70      A
ATOM   1014  CB  HIS A 135     -20.037  33.868  37.605  1.00 60.65      A
ATOM   1015  CG  HIS A 135     -19.483  34.299  36.288  1.00 60.65      A
ATOM   1016  CD2 HIS A 135     -20.090  34.643  35.129  1.00 60.65      A
ATOM   1017  ND1 HIS A 135     -18.129  34.420  36.065  1.00 60.65      A
ATOM   1018  CE1 HIS A 135     -17.924  34.821  34.823  1.00 60.65      A
ATOM   1019  NE2 HIS A 135     -19.098  34.964  34.234  1.00 60.65      A
ATOM   1020  C   HIS A 135     -19.158  35.824  38.925  1.00 73.70      A
ATOM   1021  O   HIS A 135     -18.138  36.378  39.334  1.00 73.70      A
ATOM   1022  N   ASP A 136     -20.241  36.514  38.589  1.00 66.01      A
ATOM   1023  CA  ASP A 136     -20.230  37.957  38.819  1.00 66.01      A
ATOM   1024  CB  ASP A 136     -20.599  38.762  37.562  1.00 86.73      A
ATOM   1025  CG  ASP A 136     -21.682  38.121  36.745  1.00 86.73      A
ATOM   1026  OD1 ASP A 136     -22.771  37.856  37.297  1.00 86.73      A
```

FIGURE 25 CON'T

```
ATOM   1027  OD2 ASP A 136     -21.442  37.894  35.540  1.00 86.73      A
ATOM   1028  C   ASP A 136     -21.188  38.229  39.975  1.00 66.01      A
ATOM   1029  O   ASP A 136     -20.750  38.464  41.099  1.00 66.01      A
ATOM   1030  N   GLU A 137     -22.488  38.167  39.726  1.00 48.31      A
ATOM   1031  CA  GLU A 137     -23.454  38.379  40.801  1.00 48.31      A
ATOM   1032  CB  GLU A 137     -24.469  39.455  40.392  1.00110.10      A
ATOM   1033  CG  GLU A 137     -25.060  39.267  38.999  1.00110.10      A
ATOM   1034  CD  GLU A 137     -26.069  40.347  38.631  1.00110.10      A
ATOM   1035  OE1 GLU A 137     -25.735  41.548  38.746  1.00110.10      A
ATOM   1036  OE2 GLU A 137     -27.195  39.992  38.218  1.00110.10      A
ATOM   1037  C   GLU A 137     -24.185  37.078  41.164  1.00 48.31      A
ATOM   1038  O   GLU A 137     -24.998  37.049  42.083  1.00 48.31      A
ATOM   1039  N   ASP A 138     -23.873  36.001  40.452  1.00 47.89      A
ATOM   1040  CA  ASP A 138     -24.520  34.708  40.681  1.00 47.89      A
ATOM   1041  CB  ASP A 138     -25.025  34.166  39.350  1.00 55.11      A
ATOM   1042  CG  ASP A 138     -26.057  35.069  38.721  1.00 55.11      A
ATOM   1043  OD1 ASP A 138     -27.145  35.214  39.315  1.00 55.11      A
ATOM   1044  OD2 ASP A 138     -25.775  35.640  37.646  1.00 55.11      A
ATOM   1045  C   ASP A 138     -23.631  33.663  41.353  1.00 47.89      A
ATOM   1046  O   ASP A 138     -22.409  33.753  41.313  1.00 47.89      A
ATOM   1047  N   PHE A 139     -24.254  32.674  41.979  1.00 46.35      A
ATOM   1048  CA  PHE A 139     -23.506  31.611  42.644  1.00 46.35      A
ATOM   1049  CB  PHE A 139     -23.936  31.494  44.106  1.00 44.51      A
ATOM   1050  CG  PHE A 139     -23.541  32.678  44.939  1.00 44.51      A
ATOM   1051  CD1 PHE A 139     -22.281  32.743  45.526  1.00 44.51      A

ATOM   1052  CD2 PHE A 139     -24.415  33.752  45.100  1.00 44.51      A
ATOM   1053  CE1 PHE A 139     -21.891  33.863  46.260  1.00 44.51      A
ATOM   1054  CE2 PHE A 139     -24.038  34.880  45.836  1.00 44.51      A
ATOM   1055  CZ  PHE A 139     -22.775  34.936  46.415  1.00 44.51      A
ATOM   1056  C   PHE A 139     -23.726  30.298  41.915  1.00 46.35      A
ATOM   1057  O   PHE A 139     -24.855  29.954  41.562  1.00 46.35      A
ATOM   1058  N   TYR A 140     -22.630  29.577  41.693  1.00 41.55      A
ATOM   1059  CA  TYR A 140     -22.662  28.304  40.992  1.00 41.55      A
ATOM   1060  CB  TYR A 140     -21.934  28.440  39.657  1.00 47.06      A
ATOM   1061  CG  TYR A 140     -22.594  29.410  38.703  1.00 47.06      A
ATOM   1062  CD1 TYR A 140     -23.511  28.964  37.749  1.00 47.06      A
ATOM   1063  CE1 TYR A 140     -24.139  29.857  36.881  1.00 47.06      A
ATOM   1064  CD2 TYR A 140     -22.320  30.776  38.768  1.00 47.06      A
ATOM   1065  CE2 TYR A 140     -22.942  31.677  37.911  1.00 47.06      A
ATOM   1066  CZ  TYR A 140     -23.851  31.207  36.972  1.00 47.06      A
ATOM   1067  OH  TYR A 140     -24.487  32.091  36.138  1.00 47.06      A
ATOM   1068  C   TYR A 140     -22.040  27.159  41.787  1.00 41.55      A
ATOM   1069  O   TYR A 140     -20.998  27.305  42.438  1.00 41.55      A
ATOM   1070  N   LEU A 141     -22.696  26.012  41.726  1.00 41.62      A
ATOM   1071  CA  LEU A 141     -22.220  24.834  42.410  1.00 41.62      A
ATOM   1072  CB  LEU A 141     -23.396  23.978  42.876  1.00 36.37      A
ATOM   1073  CG  LEU A 141     -22.993  22.587  43.380  1.00 36.37      A
ATOM   1074  CD1 LEU A 141     -22.221  22.707  44.680  1.00 36.37      A
ATOM   1075  CD2 LEU A 141     -24.234  21.738  43.583  1.00 36.37      A
ATOM   1076  C   LEU A 141     -21.371  24.044  41.427  1.00 41.62      A
ATOM   1077  O   LEU A 141     -21.819  23.740  40.323  1.00 41.62      A
ATOM   1078  N   VAL A 142     -20.137  23.743  41.823  1.00 39.96      A
ATOM   1079  CA  VAL A 142     -19.238  22.960  40.993  1.00 39.96      A
ATOM   1080  CB  VAL A 142     -17.763  23.401  41.169  1.00 31.71      A
ATOM   1081  CG1 VAL A 142     -16.862  22.590  40.231  1.00 31.71      A
ATOM   1082  CG2 VAL A 142     -17.613  24.898  40.886  1.00 31.71      A
```

FIGURE 25 CON'T

```
ATOM   1083  C   VAL A 142     -19.371  21.519  41.476  1.00 39.96      A
ATOM   1084  O   VAL A 142     -19.204  21.245  42.672  1.00 39.96      A
ATOM   1085  N   ILE A 143     -19.715  20.609  40.562  1.00 35.84      A
ATOM   1086  CA  ILE A 143     -19.838  19.201  40.900  1.00 35.84      A
ATOM   1087  CB  ILE A 143     -21.208  18.622  40.508  1.00 43.14      A
ATOM   1088  CG2 ILE A 143     -21.312  17.186  40.996  1.00 43.14      A
ATOM   1089  CG1 ILE A 143     -22.332  19.464  41.118  1.00 43.14      A
ATOM   1090  CD1 ILE A 143     -23.726  18.935  40.785  1.00 43.14      A
ATOM   1091  C   ILE A 143     -18.760  18.526  40.084  1.00 35.84      A
ATOM   1092  O   ILE A 143     -18.836  18.476  38.845  1.00 35.84      A
ATOM   1093  N   HIS A 144     -17.756  18.002  40.782  1.00 37.56      A
ATOM   1094  CA  HIS A 144     -16.610  17.384  40.138  1.00 37.56      A
ATOM   1095  CB  HIS A 144     -15.364  18.235  40.458  1.00 36.74      A
ATOM   1096  CG  HIS A 144     -14.069  17.660  39.965  1.00 36.74      A
ATOM   1097  CD2 HIS A 144     -12.882  17.474  40.597  1.00 36.74      A
ATOM   1098  ND1 HIS A 144     -13.888  17.214  38.672  1.00 36.74      A
ATOM   1099  CE1 HIS A 144     -12.649  16.771  38.527  1.00 36.74      A
ATOM   1100  NE2 HIS A 144     -12.017  16.919  39.681  1.00 36.74      A
ATOM   1101  C   HIS A 144     -16.425  15.937  40.565  1.00 37.56      A
ATOM   1102  O   HIS A 144     -16.318  15.619  41.759  1.00 37.56      A
ATOM   1103  N   ILE A 145     -16.387  15.060  39.565  1.00 38.15      A
ATOM   1104  CA  ILE A 145     -16.228  13.630  39.789  1.00 38.15      A
ATOM   1105  CB  ILE A 145     -16.747  12.837  38.570  1.00 37.53      A
ATOM   1106  CG2 ILE A 145     -16.476  11.354  38.765  1.00 37.53      A
ATOM   1107  CG1 ILE A 145     -18.237  13.113  38.370  1.00 37.53      A
ATOM   1108  CD1 ILE A 145     -18.797  12.562  37.054  1.00 37.53      A
ATOM   1109  C   ILE A 145     -14.764  13.253  40.033  1.00 38.15      A
ATOM   1110  O   ILE A 145     -13.888  13.527  39.201  1.00 38.15      A
ATOM   1111  N   ILE A 146     -14.512  12.605  41.169  1.00 35.02      A
ATOM   1112  CA  ILE A 146     -13.165  12.173  41.541  1.00 35.02      A
ATOM   1113  CB  ILE A 146     -12.596  13.013  42.715  1.00 39.08      A
ATOM   1114  CG2 ILE A 146     -12.316  14.451  42.250  1.00 39.08      A
ATOM   1115  CG1 ILE A 146     -13.572  12.980  43.898  1.00 39.08      A
ATOM   1116  CD1 ILE A 146     -13.026  13.632  45.202  1.00 39.08      A
ATOM   1117  C   ILE A 146     -13.192  10.706  41.968  1.00 35.02      A
ATOM   1118  O   ILE A 146     -14.263  10.098  42.046  1.00 35.02      A
ATOM   1119  N   HIS A 147     -12.025  10.143  42.266  1.00 46.27      A
ATOM   1120  CA  HIS A 147     -11.959   8.742  42.665  1.00 46.27      A
ATOM   1121  CB  HIS A 147     -11.571   7.856  41.471  1.00 43.25      A
ATOM   1122  CG  HIS A 147     -12.430   8.050  40.259  1.00 43.25      A
ATOM   1123  CD2 HIS A 147     -13.390   7.266  39.711  1.00 43.25      A
ATOM   1124  ND1 HIS A 147     -12.358   9.178  39.467  1.00 43.25      A
ATOM   1125  CE1 HIS A 147     -13.235   9.078  38.483  1.00 43.25      A
ATOM   1126  NE2 HIS A 147     -13.874   7.927  38.609  1.00 43.25      A
ATOM   1127  C   HIS A 147     -10.969   8.449  43.786  1.00 46.27      A
ATOM   1128  O   HIS A 147      -9.878   9.005  43.830  1.00 46.27      A
ATOM   1129  N   GLN A 148     -11.365   7.557  44.688  1.00 42.59      A
ATOM   1130  CA  GLN A 148     -10.494   7.123  45.761  1.00 42.59      A
ATOM   1131  CB  GLN A 148     -11.223   7.149  47.113  1.00 65.13      A
ATOM   1132  CG  GLN A 148     -11.757   8.519  47.542  1.00 65.13      A
ATOM   1133  CD  GLN A 148     -13.158   8.835  47.000  1.00 65.13      A
ATOM   1134  OE1 GLN A 148     -14.142   8.171  47.346  1.00 65.13      A
ATOM   1135  NE2 GLN A 148     -13.247   9.859  46.154  1.00 65.13      A
ATOM   1136  C   GLN A 148     -10.120   5.678  45.399  1.00 42.59      A
ATOM   1137  O   GLN A 148     -10.924   4.952  44.801  1.00 42.59      A
ATOM   1138  N   ILE A 149      -8.897   5.270  45.715  1.00 41.44      A
ATOM   1139  CA  ILE A 149      -8.469   3.890  45.461  1.00 41.44      A
```

FIGURE 25 CON'T

```
ATOM   1140  CB  ILE A 149      -7.202   3.823  44.610  1.00 42.23      A
ATOM   1141  CG2 ILE A 149      -6.783   2.372  44.433  1.00 42.23      A
ATOM   1142  CG1 ILE A 149      -7.463   4.458  43.241  1.00 42.23      A
ATOM   1143  CD1 ILE A 149      -6.203   4.648  42.403  1.00 42.23      A
ATOM   1144  C   ILE A 149      -8.182   3.315  46.850  1.00 41.44      A
ATOM   1145  O   ILE A 149      -7.272   3.772  47.542  1.00 41.44      A
ATOM   1146  N   GLN A 150      -8.969   2.321  47.251  1.00 44.13      A
ATOM   1147  CA  GLN A 150      -8.842   1.730  48.578  1.00 44.13      A
ATOM   1148  CB  GLN A 150     -10.108   2.039  49.384  1.00 49.13      A
ATOM   1149  CG  GLN A 150     -10.094   1.579  50.835  1.00 49.13      A
ATOM   1150  CD  GLN A 150     -11.403   1.878  51.546  1.00 49.13      A
ATOM   1151  OE1 GLN A 150     -11.869   3.021  51.567  1.00 49.13      A
ATOM   1152  NE2 GLN A 150     -12.005   0.851  52.134  1.00 49.13      A
ATOM   1153  C   GLN A 150      -8.593   0.230  48.603  1.00 44.13      A
ATOM   1154  O   GLN A 150      -9.333  -0.551  47.997  1.00 44.13      A
ATOM   1155  N   SER A 151      -7.555  -0.174  49.325  1.00 46.94      A
ATOM   1156  CA  SER A 151      -7.243  -1.590  49.441  1.00 46.94      A
ATOM   1157  CB  SER A 151      -5.909  -1.799  50.168  1.00 41.30      A
ATOM   1158  OG  SER A 151      -5.680  -3.188  50.382  1.00 41.30      A
ATOM   1159  C   SER A 151      -8.352  -2.297  50.218  1.00 46.94      A
ATOM   1160  O   SER A 151      -8.877  -1.763  51.196  1.00 46.94      A
ATOM   1161  N   MSE A 152      -8.714  -3.491  49.769  1.00 54.87      A
ATOM   1162  CA  MSE A 152      -9.736  -4.279  50.443  1.00 54.87      A
ATOM   1163  CB  MSE A 152     -10.521  -5.115  49.422  1.00 70.62      A
ATOM   1164  CG  MSE A 152     -11.422  -4.294  48.492  1.00 70.62      A
ATOM   1165  SE  MSE A 152     -12.737  -3.231  49.456  1.00 70.62      A
ATOM   1166  CE  MSE A 152     -11.729  -1.594  49.615  1.00 70.62      A
ATOM   1167  C   MSE A 152      -9.043  -5.185  51.474  1.00 54.87      A
ATOM   1168  O   MSE A 152      -9.695  -5.909  52.229  1.00 54.87      A
ATOM   1169  N   LYS A 153      -7.712  -5.127  51.492  1.00 50.97      A
ATOM   1170  CA  LYS A 153      -6.897  -5.899  52.431  1.00 50.97      A
ATOM   1171  CB  LYS A 153      -5.841  -6.727  51.693  1.00 90.19      A
ATOM   1172  CG  LYS A 153      -6.356  -7.962  50.985  1.00 90.19      A
ATOM   1173  CD  LYS A 153      -5.197  -8.695  50.325  1.00 90.19      A
ATOM   1174  CE  LYS A 153      -5.638  -9.999  49.685  1.00 90.19      A
ATOM   1175  NZ  LYS A 153      -4.519 -10.624  48.923  1.00 90.19      A
ATOM   1176  C   LYS A 153      -6.179  -4.946  53.382  1.00 50.97      A
ATOM   1177  O   LYS A 153      -5.703  -3.885  52.973  1.00 50.97      A
ATOM   1178  N   THR A 154      -6.101  -5.326  54.651  1.00 48.31      A
ATOM   1179  CA  THR A 154      -5.426  -4.501  55.640  1.00 48.31      A

ATOM   1180  CB  THR A 154      -5.487  -5.139  57.047  1.00 46.93      A
ATOM   1181  OG1 THR A 154      -4.889  -6.442  56.996  1.00 46.93      A
ATOM   1182  CG2 THR A 154      -6.932  -5.248  57.539  1.00 46.93      A
ATOM   1183  C   THR A 154      -3.959  -4.381  55.247  1.00 48.31      A
ATOM   1184  O   THR A 154      -3.433  -5.224  54.524  1.00 48.31      A
ATOM   1185  N   LEU A 155      -3.306  -3.327  55.722  1.00 49.03      A
ATOM   1186  CA  LEU A 155      -1.896  -3.112  55.444  1.00 49.03      A
ATOM   1187  CB  LEU A 155      -1.424  -1.837  56.155  1.00 41.52      A
ATOM   1188  CG  LEU A 155       0.077  -1.527  56.127  1.00 41.52      A
ATOM   1189  CD1 LEU A 155       0.559  -1.395  54.671  1.00 41.52      A
ATOM   1190  CD2 LEU A 155       0.358  -0.244  56.912  1.00 41.52      A
ATOM   1191  C   LEU A 155      -1.082  -4.327  55.926  1.00 49.03      A
ATOM   1192  O   LEU A 155      -0.156  -4.778  55.249  1.00 49.03      A
ATOM   1193  N   TRP A 156      -1.440  -4.862  57.092  1.00 44.28      A
ATOM   1194  CA  TRP A 156      -0.730  -6.021  57.648  1.00 44.28      A
ATOM   1195  CB  TRP A 156      -1.290  -6.371  59.035  1.00 57.24      A
```

FIGURE 25 CON'T

```
ATOM   1196  CG  TRP A 156      -0.456  -7.355  59.831  1.00 57.24      A
ATOM   1197  CD2 TRP A 156       0.957  -7.288  60.091  1.00 57.24      A
ATOM   1198  CE2 TRP A 156       1.281  -8.380  60.931  1.00 57.24      A
ATOM   1199  CE3 TRP A 156       1.977  -6.413  59.700  1.00 57.24      A
ATOM   1200  CD1 TRP A 156      -0.912  -8.458  60.502  1.00 57.24      A
ATOM   1201  NE1 TRP A 156       0.124  -9.075  61.164  1.00 57.24      A
ATOM   1202  CZ2 TRP A 156       2.584  -8.619  61.388  1.00 57.24      A
ATOM   1203  CZ3 TRP A 156       3.277  -6.651  60.156  1.00 57.24      A
ATOM   1204  CH2 TRP A 156       3.566  -7.747  60.992  1.00 57.24      A
ATOM   1205  C   TRP A 156      -0.852  -7.227  56.709  1.00 44.28      A
ATOM   1206  O   TRP A 156       0.144  -7.898  56.424  1.00 44.28      A
ATOM   1207  N   GLU A 157      -2.066  -7.498  56.229  1.00 54.86      A
ATOM   1208  CA  GLU A 157      -2.292  -8.615  55.304  1.00 54.86      A
ATOM   1209  CB  GLU A 157      -3.791  -8.805  55.032  1.00 89.57      A
ATOM   1210  CG  GLU A 157      -4.613  -9.378  56.192  1.00 89.57      A
ATOM   1211  CD  GLU A 157      -4.183 -10.784  56.607  1.00 89.57      A
ATOM   1212  OE1 GLU A 157      -3.999 -11.649  55.722  1.00 89.57      A
ATOM   1213  OE2 GLU A 157      -4.041 -11.028  57.826  1.00 89.57      A
ATOM   1214  C   GLU A 157      -1.563  -8.404  53.968  1.00 54.86      A
ATOM   1215  O   GLU A 157      -1.016  -9.353  53.396  1.00 54.86      A
ATOM   1216  N   LEU A 158      -1.559  -7.166  53.474  1.00 65.79      A
ATOM   1217  CA  LEU A 158      -0.902  -6.843  52.203  1.00 65.79      A
ATOM   1218  CB  LEU A 158      -1.041  -5.350  51.858  1.00 58.91      A
ATOM   1219  CG  LEU A 158      -2.381  -4.781  51.380  1.00 58.91      A
ATOM   1220  CD1 LEU A 158      -2.184  -3.311  51.006  1.00 58.91      A
ATOM   1221  CD2 LEU A 158      -2.892  -5.567  50.166  1.00 58.91      A
ATOM   1222  C   LEU A 158       0.576  -7.183  52.202  1.00 65.79      A
ATOM   1223  O   LEU A 158       1.114  -7.635  51.194  1.00 65.79      A
ATOM   1224  N   VAL A 159       1.243  -6.951  53.326  1.00 53.76      A
ATOM   1225  CA  VAL A 159       2.667  -7.229  53.397  1.00 53.76      A
ATOM   1226  CB  VAL A 159       3.390  -6.165  54.245  1.00 42.90      A
ATOM   1227  CG1 VAL A 159       3.275  -4.826  53.567  1.00 42.90      A
ATOM   1228  CG2 VAL A 159       2.788  -6.089  55.654  1.00 42.90      A
ATOM   1229  C   VAL A 159       2.982  -8.621  53.927  1.00 53.76      A
ATOM   1230  O   VAL A 159       4.126  -8.924  54.260  1.00 53.76      A
ATOM   1231  N   ASN A 160       1.968  -9.474  53.989  1.00 60.19      A
ATOM   1232  CA  ASN A 160       2.155 -10.833  54.472  1.00 60.19      A
ATOM   1233  CB  ASN A 160       3.110 -11.585  53.546  1.00 75.15      A
ATOM   1234  CG  ASN A 160       2.628 -11.600  52.110  1.00 75.15      A
ATOM   1235  OD1 ASN A 160       1.543 -12.104  51.814  1.00 75.15      A
ATOM   1236  ND2 ASN A 160       3.432 -11.041  51.209  1.00 75.15      A
ATOM   1237  C   ASN A 160       2.686 -10.877  55.904  1.00 60.19      A
ATOM   1238  O   ASN A 160       3.582 -11.666  56.220  1.00 60.19      A
ATOM   1239  N   LYS A 161       2.133 -10.021  56.759  1.00 76.52      A
ATOM   1240  CA  LYS A 161       2.514  -9.969  58.168  1.00 76.52      A
ATOM   1241  CB  LYS A 161       1.879 -11.145  58.918  1.00 68.87      A
ATOM   1242  CG  LYS A 161       0.359 -11.203  58.856  1.00 68.87      A
ATOM   1243  CD  LYS A 161      -0.122 -12.637  59.038  1.00 68.87      A
ATOM   1244  CE  LYS A 161      -1.642 -12.751  59.103  1.00 68.87      A
ATOM   1245  NZ  LYS A 161      -2.174 -12.601  60.493  1.00 68.87      A
ATOM   1246  C   LYS A 161       4.025  -9.994  58.391  1.00 76.52      A
ATOM   1247  O   LYS A 161       4.496 -10.520  59.396  1.00 76.52      A
ATOM   1248  N   ASP A 162       4.786  -9.431  57.460  1.00 63.39      A
ATOM   1249  CA  ASP A 162       6.237  -9.412  57.602  1.00 63.39      A
ATOM   1250  CB  ASP A 162       6.905  -9.953  56.333  1.00 91.30      A
ATOM   1251  CG  ASP A 162       8.422  -9.923  56.413  1.00 91.30      A
ATOM   1252  OD1 ASP A 162       8.985 -10.438  57.402  1.00 91.30      A
```

FIGURE 25 CON'T

```
ATOM   1253  OD2 ASP A 162       9.053  -9.387  55.481  1.00 91.30      A
ATOM   1254  C   ASP A 162       6.747  -8.006  57.897  1.00 63.39      A
ATOM   1255  O   ASP A 162       6.662  -7.116  57.052  1.00 63.39      A
ATOM   1256  N   PRO A 163       7.288  -7.789  59.109  1.00 61.09      A
ATOM   1257  CD  PRO A 163       7.515  -8.786  60.172  1.00 64.53      A
ATOM   1258  CA  PRO A 163       7.810  -6.477  59.506  1.00 61.09      A
ATOM   1259  CB  PRO A 163       8.491  -6.766  60.843  1.00 64.53      A
ATOM   1260  CG  PRO A 163       7.692  -7.911  61.391  1.00 64.53      A
ATOM   1261  C   PRO A 163       8.794  -5.944  58.474  1.00 61.09      A
ATOM   1262  O   PRO A 163       8.822  -4.743  58.191  1.00 61.09      A
ATOM   1263  N   LYS A 164       9.593  -6.855  57.923  1.00135.00      A
ATOM   1264  CA  LYS A 164      10.599  -6.522  56.920  1.00135.00      A
ATOM   1265  CB  LYS A 164      11.804  -7.460  57.059  1.00129.94      A
ATOM   1266  CG  LYS A 164      13.137  -6.851  56.634  1.00129.94      A
ATOM   1267  CD  LYS A 164      13.131  -6.404  55.182  1.00129.94      A
ATOM   1268  CE  LYS A 164      14.456  -5.774  54.796  1.00129.94      A
ATOM   1269  NZ  LYS A 164      15.582  -6.728  54.973  1.00129.94      A
ATOM   1270  C   LYS A 164      10.004  -6.635  55.515  1.00135.00      A
ATOM   1271  O   LYS A 164      10.511  -7.359  54.658  1.00135.00      A
ATOM   1272  N   GLU A 165       8.913  -5.909  55.305  1.00 64.61      A
ATOM   1273  CA  GLU A 165       8.196  -5.857  54.037  1.00 64.61      A
ATOM   1274  CB  GLU A 165       7.451  -7.168  53.770  1.00 86.95      A
ATOM   1275  CG  GLU A 165       6.534  -7.111  52.556  1.00 86.95      A
ATOM   1276  CD  GLU A 165       6.123  -8.486  52.044  1.00 86.95      A
ATOM   1277  OE1 GLU A 165       5.166  -8.559  51.242  1.00 86.95      A
ATOM   1278  OE2 GLU A 165       6.760  -9.489  52.433  1.00 86.95      A
ATOM   1279  C   GLU A 165       7.211  -4.709  54.210  1.00 64.61      A
ATOM   1280  O   GLU A 165       6.870  -4.003  53.264  1.00 64.61      A
ATOM   1281  N   LEU A 166       6.774  -4.536  55.452  1.00 51.26      A
ATOM   1282  CA  LEU A 166       5.852  -3.478  55.829  1.00 51.26      A
ATOM   1283  CB  LEU A 166       5.386  -3.704  57.273  1.00 79.12      A
ATOM   1284  CG  LEU A 166       4.373  -2.777  57.951  1.00 79.12      A
ATOM   1285  CD1 LEU A 166       4.037  -3.349  59.319  1.00 79.12      A
ATOM   1286  CD2 LEU A 166       4.931  -1.378  58.104  1.00 79.12      A
ATOM   1287  C   LEU A 166       6.599  -2.152  55.719  1.00 51.26      A
ATOM   1288  O   LEU A 166       6.126  -1.203  55.091  1.00 51.26      A
ATOM   1289  N   GLU A 167       7.773  -2.088  56.334  1.00 58.64      A
ATOM   1290  CA  GLU A 167       8.564  -0.867  56.298  1.00 58.64      A
ATOM   1291  CB  GLU A 167       9.827  -1.021  57.151  1.00 82.34      A
ATOM   1292  CG  GLU A 167      10.730   0.203  57.131  1.00 82.34      A
ATOM   1293  CD  GLU A 167      11.960   0.042  58.003  1.00 82.34      A
ATOM   1294  OE1 GLU A 167      12.662  -0.982  57.856  1.00 82.34      A
ATOM   1295  OE2 GLU A 167      12.227   0.943  58.829  1.00 82.34      A
ATOM   1296  C   GLU A 167       8.944  -0.520  54.859  1.00 58.64      A
ATOM   1297  O   GLU A 167       9.042   0.654  54.501  1.00 58.64      A
ATOM   1298  N   GLU A 168       9.161  -1.545  54.039  1.00 64.16      A
ATOM   1299  CA  GLU A 168       9.520  -1.331  52.643  1.00 64.16      A
ATOM   1300  CB  GLU A 168       9.900  -2.657  51.971  1.00106.41      A
ATOM   1301  CG  GLU A 168      11.256  -3.215  52.395  1.00106.41      A
ATOM   1302  CD  GLU A 168      11.577  -4.551  51.739  1.00106.41      A
ATOM   1303  OE1 GLU A 168      11.561  -4.626  50.493  1.00106.41      A
ATOM   1304  OE2 GLU A 168      11.851  -5.528  52.470  1.00106.41      A
ATOM   1305  C   GLU A 168       8.335  -0.702  51.923  1.00 64.16      A
ATOM   1306  O   GLU A 168       8.500   0.212  51.118  1.00 64.16      A
ATOM   1307  N   PHE A 169       7.139  -1.195  52.232  1.00 55.37      A

ATOM   1308  CA  PHE A 169       5.915  -0.684  51.628  1.00 55.37      A
```

FIGURE 25 CON'T

```
ATOM   1309  CB  PHE A 169       4.706  -1.451  52.177  1.00 53.88      A
ATOM   1310  CG  PHE A 169       3.415  -1.143  51.466  1.00 53.88      A
ATOM   1311  CD1 PHE A 169       3.052  -1.845  50.316  1.00 53.88      A
ATOM   1312  CD2 PHE A 169       2.567  -0.143  51.938  1.00 53.88      A
ATOM   1313  CE1 PHE A 169       1.862  -1.556  49.649  1.00 53.88      A
ATOM   1314  CE2 PHE A 169       1.374   0.157  51.279  1.00 53.88      A
ATOM   1315  CZ  PHE A 169       1.018  -0.549  50.133  1.00 53.88      A
ATOM   1316  C   PHE A 169       5.775   0.813  51.950  1.00 55.37      A
ATOM   1317  O   PHE A 169       5.673   1.652  51.050  1.00 55.37      A
ATOM   1318  N   LEU A 170       5.787   1.136  53.239  1.00 50.99      A
ATOM   1319  CA  LEU A 170       5.656   2.518  53.696  1.00 50.99      A
ATOM   1320  CB  LEU A 170       5.898   2.598  55.209  1.00 58.50      A
ATOM   1321  CG  LEU A 170       4.683   2.588  56.149  1.00 58.50      A
ATOM   1322  CD1 LEU A 170       3.532   1.796  55.560  1.00 58.50      A
ATOM   1323  CD2 LEU A 170       5.112   2.012  57.490  1.00 58.50      A
ATOM   1324  C   LEU A 170       6.602   3.466  52.982  1.00 50.99      A
ATOM   1325  O   LEU A 170       6.200   4.541  52.553  1.00 50.99      A
ATOM   1326  N   MSE A 171       7.858   3.052  52.859  1.00 63.39      A
ATOM   1327  CA  MSE A 171       8.885   3.858  52.210  1.00 63.39      A
ATOM   1328  CB  MSE A 171      10.254   3.196  52.393  1.00 80.35      A
ATOM   1329  CG  MSE A 171      10.648   2.987  53.846  1.00 80.35      A
ATOM   1330  SE  MSE A 171      12.434   2.258  54.064  1.00 80.35      A
ATOM   1331  CE  MSE A 171      12.087   0.420  53.595  1.00 80.35      A
ATOM   1332  C   MSE A 171       8.647   4.110  50.718  1.00 63.39      A
ATOM   1333  O   MSE A 171       8.844   5.224  50.232  1.00 63.39      A
ATOM   1334  N   THR A 172       8.232   3.073  49.998  1.00 62.45      A
ATOM   1335  CA  THR A 172       8.001   3.187  48.564  1.00 62.45      A
ATOM   1336  CB  THR A 172       7.875   1.800  47.902  1.00 87.89      A
ATOM   1337  OG1 THR A 172       6.680   1.159  48.360  1.00 87.89      A
ATOM   1338  CG2 THR A 172       9.075   0.931  48.247  1.00 87.89      A
ATOM   1339  C   THR A 172       6.761   3.998  48.195  1.00 62.45      A
ATOM   1340  O   THR A 172       6.779   4.736  47.213  1.00 62.45      A
ATOM   1341  N   HIS A 173       5.692   3.865  48.980  1.00 52.70      A
ATOM   1342  CA  HIS A 173       4.441   4.579  48.704  1.00 52.70      A
ATOM   1343  CB  HIS A 173       3.254   3.647  48.936  1.00 59.03      A
ATOM   1344  CG  HIS A 173       3.262   2.436  48.058  1.00 59.03      A
ATOM   1345  CD2 HIS A 173       3.381   1.120  48.354  1.00 59.03      A
ATOM   1346  ND1 HIS A 173       3.154   2.511  46.686  1.00 59.03      A
ATOM   1347  CE1 HIS A 173       3.204   1.294  46.176  1.00 59.03      A
ATOM   1348  NE2 HIS A 173       3.342   0.432  47.166  1.00 59.03      A
ATOM   1349  C   HIS A 173       4.292   5.829  49.556  1.00 52.70      A
ATOM   1350  O   HIS A 173       3.222   6.441  49.614  1.00 52.70      A
ATOM   1351  N   LYS A 174       5.391   6.207  50.195  1.00 50.21      A
ATOM   1352  CA  LYS A 174       5.441   7.361  51.087  1.00 50.21      A
ATOM   1353  CB  LYS A 174       6.905   7.677  51.434  1.00 67.16      A
ATOM   1354  CG  LYS A 174       7.128   9.042  52.091  1.00 67.16      A
ATOM   1355  CD  LYS A 174       8.586   9.223  52.519  1.00 67.16      A
ATOM   1356  CE  LYS A 174       8.982  10.701  52.637  1.00 67.16      A
ATOM   1357  NZ  LYS A 174       8.142  11.497  53.570  1.00 67.16      A
ATOM   1358  C   LYS A 174       4.755   8.639  50.615  1.00 50.21      A
ATOM   1359  O   LYS A 174       3.994   9.249  51.366  1.00 50.21      A
ATOM   1360  N   GLU A 175       5.034   9.040  49.379  1.00 50.65      A
ATOM   1361  CA  GLU A 175       4.494  10.277  48.817  1.00 50.65      A
ATOM   1362  CB  GLU A 175       5.123  10.533  47.444  1.00 95.83      A
ATOM   1363  CG  GLU A 175       6.647  10.566  47.443  1.00 95.83      A
ATOM   1364  CD  GLU A 175       7.220  11.504  48.494  1.00 95.83      A
ATOM   1365  OE1 GLU A 175       6.744  12.656  48.594  1.00 95.83      A
```

FIGURE 25 CON'T

```
ATOM   1366  OE2 GLU A 175       8.153  11.089  49.215  1.00 95.83      A
ATOM   1367  C   GLU A 175       2.974  10.395  48.695  1.00 50.65      A
ATOM   1368  O   GLU A 175       2.424  11.487  48.840  1.00 50.65      A
ATOM   1369  N   ASN A 176       2.289   9.288  48.443  1.00 41.11      A
ATOM   1370  CA  ASN A 176       0.839   9.349  48.283  1.00 41.11      A
ATOM   1371  CB  ASN A 176       0.492   8.969  46.849  1.00 58.07      A
ATOM   1372  CG  ASN A 176       1.348   9.699  45.841  1.00 58.07      A
ATOM   1373  OD1 ASN A 176       1.352  10.927  45.792  1.00 58.07      A
ATOM   1374  ND2 ASN A 176       2.085   8.949  45.035  1.00 58.07      A
ATOM   1375  C   ASN A 176       0.010   8.481  49.239  1.00 41.11      A
ATOM   1376  O   ASN A 176      -1.206   8.637  49.329  1.00 41.11      A
ATOM   1377  N   LEU A 177       0.667   7.584  49.962  1.00 43.75      A
ATOM   1378  CA  LEU A 177      -0.051   6.680  50.849  1.00 43.75      A
ATOM   1379  CB  LEU A 177       0.891   5.602  51.381  1.00 45.30      A
ATOM   1380  CG  LEU A 177       0.243   4.561  52.296  1.00 45.30      A
ATOM   1381  CD1 LEU A 177      -0.659   3.666  51.469  1.00 45.30      A
ATOM   1382  CD2 LEU A 177       1.322   3.732  52.998  1.00 45.30      A
ATOM   1383  C   LEU A 177      -0.770   7.308  52.026  1.00 43.75      A
ATOM   1384  O   LEU A 177      -0.230   8.153  52.744  1.00 43.75      A
ATOM   1385  N   MSE A 178      -2.015   6.887  52.197  1.00 41.72      A
ATOM   1386  CA  MSE A 178      -2.826   7.321  53.320  1.00 41.72      A
ATOM   1387  CB  MSE A 178      -3.960   8.251  52.887  1.00 57.42      A
ATOM   1388  CG  MSE A 178      -3.480   9.643  52.493  1.00 57.42      A
ATOM   1389  SE  MSE A 178      -4.933  10.844  52.058  1.00 57.42      A
ATOM   1390  CE  MSE A 178      -5.535   9.981  50.427  1.00 57.42      A
ATOM   1391  C   MSE A 178      -3.366   6.017  53.886  1.00 41.72      A
ATOM   1392  O   MSE A 178      -3.425   5.009  53.183  1.00 41.72      A
ATOM   1393  N   LEU A 179      -3.732   6.034  55.160  1.00 41.26      A
ATOM   1394  CA  LEU A 179      -4.234   4.841  55.817  1.00 41.26      A
ATOM   1395  CB  LEU A 179      -3.202   4.351  56.835  1.00 39.11      A
ATOM   1396  CG  LEU A 179      -1.915   3.859  56.180  1.00 39.11      A
ATOM   1397  CD1 LEU A 179      -0.833   3.578  57.237  1.00 39.11      A
ATOM   1398  CD2 LEU A 179      -2.244   2.605  55.371  1.00 39.11      A
ATOM   1399  C   LEU A 179      -5.556   5.123  56.490  1.00 41.26      A
ATOM   1400  O   LEU A 179      -5.667   6.054  57.282  1.00 41.26      A
ATOM   1401  N   LYS A 180      -6.550   4.310  56.155  1.00 43.84      A
ATOM   1402  CA  LYS A 180      -7.895   4.435  56.691  1.00 43.84      A
ATOM   1403  CB  LYS A 180      -8.919   4.242  55.568  1.00 54.71      A
ATOM   1404  CG  LYS A 180     -10.357   4.230  56.045  1.00 54.71      A
ATOM   1405  CD  LYS A 180     -11.334   3.877  54.927  1.00 54.71      A
ATOM   1406  CE  LYS A 180     -11.773   5.110  54.150  1.00 54.71      A
ATOM   1407  NZ  LYS A 180     -10.607   5.837  53.579  1.00 54.71      A
ATOM   1408  C   LYS A 180      -8.126   3.394  57.793  1.00 43.84      A
ATOM   1409  O   LYS A 180      -7.940   2.197  57.581  1.00 43.84      A
ATOM   1410  N   ASP A 181      -8.527   3.860  58.969  1.00 49.38      A
ATOM   1411  CA  ASP A 181      -8.777   2.973  60.098  1.00 49.38      A
ATOM   1412  CB  ASP A 181      -8.667   3.764  61.410  1.00 54.56      A
ATOM   1413  CG  ASP A 181      -8.805   2.884  62.648  1.00 54.56      A
ATOM   1414  OD1 ASP A 181      -8.441   3.347  63.753  1.00 54.56      A
ATOM   1415  OD2 ASP A 181      -9.281   1.738  62.522  1.00 54.56      A
ATOM   1416  C   ASP A 181     -10.167   2.356  59.956  1.00 49.38      A
ATOM   1417  O   ASP A 181     -11.151   2.898  60.458  1.00 49.38      A
ATOM   1418  N   ILE A 182     -10.243   1.224  59.264  1.00 52.94      A
ATOM   1419  CA  ILE A 182     -11.520   0.553  59.066  1.00 52.94      A
ATOM   1420  CB  ILE A 182     -11.441  -0.521  57.951  1.00 46.44      A
ATOM   1421  CG2 ILE A 182     -11.239   0.144  56.593  1.00 46.44      A
ATOM   1422  CG1 ILE A 182     -10.293  -1.489  58.228  1.00 46.44      A
```

FIGURE 25 CON'T

```
ATOM   1423  CD1 ILE A 182     -10.327  -2.717  57.343  1.00 46.44      A
ATOM   1424  C   ILE A 182     -12.013  -0.111  60.353  1.00 52.94      A
ATOM   1425  O   ILE A 182     -13.139  -0.600  60.417  1.00 52.94      A
ATOM   1426  N   ALA A 183     -11.167  -0.135  61.376  1.00 63.47      A
ATOM   1427  CA  ALA A 183     -11.559  -0.731  62.645  1.00 63.47      A
ATOM   1428  CB  ALA A 183     -10.338  -1.238  63.385  1.00 49.82      A
ATOM   1429  C   ALA A 183     -12.274   0.332  63.468  1.00 63.47      A
ATOM   1430  O   ALA A 183     -12.640   0.102  64.620  1.00 63.47      A
ATOM   1431  N   SER A 184     -12.466   1.501  62.863  1.00 73.28      A
ATOM   1432  CA  SER A 184     -13.137   2.620  63.518  1.00 73.28      A
ATOM   1433  CB  SER A 184     -12.217   3.844  63.538  1.00 66.59      A
ATOM   1434  OG  SER A 184     -12.923   5.004  63.934  1.00 66.59      A
ATOM   1435  C   SER A 184     -14.434   2.970  62.793  1.00 73.28      A

ATOM   1436  O   SER A 184     -14.502   2.909  61.568  1.00 73.28      A
ATOM   1437  N   PRO A 185     -15.481   3.342  63.546  1.00 71.36      A
ATOM   1438  CD  PRO A 185     -15.533   3.473  65.012  1.00 73.07      A
ATOM   1439  CA  PRO A 185     -16.770   3.697  62.947  1.00 71.36      A
ATOM   1440  CB  PRO A 185     -17.687   3.820  64.159  1.00 73.07      A
ATOM   1441  CG  PRO A 185     -16.764   4.325  65.213  1.00 73.07      A
ATOM   1442  C   PRO A 185     -16.693   4.989  62.136  1.00 71.36      A
ATOM   1443  O   PRO A 185     -17.577   5.277  61.329  1.00 71.36      A
ATOM   1444  N   LEU A 186     -15.631   5.760  62.350  1.00 64.31      A
ATOM   1445  CA  LEU A 186     -15.443   7.017  61.631  1.00 64.31      A
ATOM   1446  CB  LEU A 186     -14.856   8.082  62.565  1.00 71.48      A
ATOM   1447  CG  LEU A 186     -15.821   8.663  63.607  1.00 71.48      A
ATOM   1448  CD1 LEU A 186     -15.070   9.585  64.555  1.00 71.48      A
ATOM   1449  CD2 LEU A 186     -16.944   9.419  62.899  1.00 71.48      A
ATOM   1450  C   LEU A 186     -14.555   6.867  60.395  1.00 64.31      A
ATOM   1451  O   LEU A 186     -14.430   7.798  59.601  1.00 64.31      A
ATOM   1452  N   LYS A 187     -13.948   5.695  60.232  1.00 57.82      A
ATOM   1453  CA  LYS A 187     -13.078   5.437  59.087  1.00 57.82      A
ATOM   1454  CB  LYS A 187     -13.910   5.246  57.816  1.00 72.64      A
ATOM   1455  CG  LYS A 187     -14.565   3.884  57.699  1.00 72.64      A
ATOM   1456  CD  LYS A 187     -15.571   3.645  58.800  1.00 72.64      A
ATOM   1457  CE  LYS A 187     -16.206   2.267  58.671  1.00 72.64      A
ATOM   1458  NZ  LYS A 187     -15.194   1.181  58.793  1.00 72.64      A
ATOM   1459  C   LYS A 187     -12.102   6.586  58.883  1.00 57.82      A
ATOM   1460  O   LYS A 187     -11.776   6.942  57.752  1.00 57.82      A
ATOM   1461  N   THR A 188     -11.639   7.163  59.989  1.00 51.63      A
ATOM   1462  CA  THR A 188     -10.706   8.278  59.934  1.00 51.63      A
ATOM   1463  CB  THR A 188     -10.268   8.682  61.350  1.00 56.12      A
ATOM   1464  OG1 THR A 188     -11.434   8.904  62.155  1.00 56.12      A
ATOM   1465  CG2 THR A 188      -9.430   9.955  61.311  1.00 56.12      A
ATOM   1466  C   THR A 188      -9.482   7.924  59.096  1.00 51.63      A
ATOM   1467  O   THR A 188      -8.932   6.822  59.203  1.00 51.63      A
ATOM   1468  N   VAL A 189      -9.064   8.870  58.261  1.00 52.14      A
ATOM   1469  CA  VAL A 189      -7.920   8.687  57.373  1.00 52.14      A
ATOM   1470  CB  VAL A 189      -8.211   9.301  55.989  1.00 43.84      A
ATOM   1471  CG1 VAL A 189      -7.013   9.119  55.072  1.00 43.84      A
ATOM   1472  CG2 VAL A 189      -9.458   8.654  55.395  1.00 43.84      A
ATOM   1473  C   VAL A 189      -6.680   9.338  57.956  1.00 52.14      A
ATOM   1474  O   VAL A 189      -6.745  10.449  58.468  1.00 52.14      A
ATOM   1475  N   TYR A 190      -5.547   8.652  57.857  1.00 50.61      A
ATOM   1476  CA  TYR A 190      -4.293   9.156  58.405  1.00 50.61      A
ATOM   1477  CB  TYR A 190      -3.860   8.288  59.593  1.00 52.28      A
ATOM   1478  CG  TYR A 190      -4.853   8.208  60.725  1.00 52.28      A
```

FIGURE 25 CON'T

ATOM	1479	CD1	TYR	A	190	-4.700	8.995	61.872	1.00	52.28	A
ATOM	1480	CE1	TYR	A	190	-5.597	8.883	62.946	1.00	52.28	A
ATOM	1481	CD2	TYR	A	190	-5.928	7.316	60.672	1.00	52.28	A
ATOM	1482	CE2	TYR	A	190	-6.821	7.197	61.727	1.00	52.28	A
ATOM	1483	CZ	TYR	A	190	-6.649	7.980	62.862	1.00	52.28	A
ATOM	1484	OH	TYR	A	190	-7.519	7.842	63.916	1.00	52.28	A
ATOM	1485	C	TYR	A	190	-3.143	9.165	57.405	1.00	50.61	A
ATOM	1486	O	TYR	A	190	-3.209	8.524	56.352	1.00	50.61	A
ATOM	1487	N	LYS	A	191	-2.083	9.884	57.767	1.00	61.17	A
ATOM	1488	CA	LYS	A	191	-0.866	9.968	56.971	1.00	61.17	A
ATOM	1489	CB	LYS	A	191	-0.555	11.415	56.575	1.00	87.12	A
ATOM	1490	CG	LYS	A	191	-1.447	12.009	55.499	1.00	87.12	A
ATOM	1491	CD	LYS	A	191	-0.849	13.318	54.987	1.00	87.12	A
ATOM	1492	CE	LYS	A	191	-1.673	13.932	53.862	1.00	87.12	A
ATOM	1493	NZ	LYS	A	191	-2.996	14.428	54.329	1.00	87.12	A
ATOM	1494	C	LYS	A	191	0.253	9.456	57.874	1.00	61.17	A
ATOM	1495	O	LYS	A	191	0.530	10.040	58.918	1.00	61.17	A
ATOM	1496	N	PRO	A	192	0.911	8.359	57.488	1.00	58.43	A
ATOM	1497	CD	PRO	A	192	0.748	7.583	56.245	1.00	45.01	A
ATOM	1498	CA	PRO	A	192	1.996	7.826	58.324	1.00	58.43	A
ATOM	1499	CB	PRO	A	192	2.383	6.536	57.608	1.00	45.01	A
ATOM	1500	CG	PRO	A	192	2.068	6.855	56.155	1.00	45.01	A
ATOM	1501	C	PRO	A	192	3.178	8.789	58.475	1.00	58.43	A
ATOM	1502	O	PRO	A	192	3.603	9.409	57.501	1.00	58.43	A
ATOM	1503	N	CYS	A	193	3.695	8.908	59.702	1.00	55.22	A
ATOM	1504	CA	CYS	A	193	4.823	9.789	60.000	1.00	55.22	A
ATOM	1505	CB	CYS	A	193	4.886	10.104	61.494	1.00	68.19	A
ATOM	1506	SG	CYS	A	193	3.616	11.226	62.072	1.00	68.19	A
ATOM	1507	C	CYS	A	193	6.139	9.167	59.574	1.00	55.22	A
ATOM	1508	O	CYS	A	193	6.296	7.947	59.601	1.00	55.22	A
ATOM	1509	N	PHE	A	194	7.088	10.010	59.187	1.00	60.62	A
ATOM	1510	CA	PHE	A	194	8.387	9.531	58.740	1.00	60.62	A
ATOM	1511	CB	PHE	A	194	8.525	9.752	57.228	1.00	53.49	A
ATOM	1512	CG	PHE	A	194	7.899	8.667	56.400	1.00	53.49	A
ATOM	1513	CD1	PHE	A	194	8.615	7.514	56.089	1.00	53.49	A
ATOM	1514	CD2	PHE	A	194	6.586	8.784	55.953	1.00	53.49	A
ATOM	1515	CE1	PHE	A	194	8.029	6.486	55.340	1.00	53.49	A
ATOM	1516	CE2	PHE	A	194	5.990	7.767	55.204	1.00	53.49	A
ATOM	1517	CZ	PHE	A	194	6.711	6.617	54.897	1.00	53.49	A
ATOM	1518	C	PHE	A	194	9.550	10.203	59.461	1.00	60.62	A
ATOM	1519	O	PHE	A	194	9.435	11.340	59.932	1.00	60.62	A
ATOM	1520	N	GLU	A	195	10.664	9.480	59.548	1.00	69.72	A
ATOM	1521	CA	GLU	A	195	11.875	9.991	60.179	1.00	69.72	A
ATOM	1522	CB	GLU	A	195	13.003	8.965	60.048	1.00108.01		A
ATOM	1523	CG	GLU	A	195	13.893	8.837	61.269	1.00108.01		A
ATOM	1524	CD	GLU	A	195	13.215	8.091	62.401	1.00108.01		A
ATOM	1525	OE1	GLU	A	195	12.949	6.880	62.241	1.00108.01		A
ATOM	1526	OE2	GLU	A	195	12.944	8.715	63.449	1.00108.01		A
ATOM	1527	C	GLU	A	195	12.218	11.238	59.368	1.00	69.72	A
ATOM	1528	O	GLU	A	195	12.658	11.132	58.221	1.00	69.72	A
ATOM	1529	N	GLU	A	196	11.999	12.408	59.960	1.00	89.83	A
ATOM	1530	CA	GLU	A	196	12.249	13.685	59.293	1.00	89.83	A
ATOM	1531	CB	GLU	A	196	12.380	14.795	60.339	1.00117.08		A
ATOM	1532	CG	GLU	A	196	12.270	16.203	59.776	1.00117.08		A
ATOM	1533	CD	GLU	A	196	12.091	17.247	60.863	1.00117.08		A
ATOM	1534	OE1	GLU	A	196	12.999	17.395	61.708	1.00117.08		A
ATOM	1535	OE2	GLU	A	196	11.037	17.918	60.874	1,00117.08		A

FIGURE 25 CON'T

```
ATOM   1536  C   GLU A 196      13.471  13.685  58.372  1.00 89.83      A
ATOM   1537  O   GLU A 196      14.540  13.187  58.731  1.00 89.83      A
ATOM   1538  N   TYR A 197      13.289  14.248  57.178  1.00 86.59      A
ATOM   1539  CA  TYR A 197      14.341  14.339  56.167  1.00 86.59      A
ATOM   1540  CB  TYR A 197      15.546  15.112  56.715  1.00103.42      A
ATOM   1541  CG  TYR A 197      15.226  16.507  57.201  1.00103.42      A
ATOM   1542  CD1 TYR A 197      14.431  17.365  56.444  1.00103.42      A
ATOM   1543  CE1 TYR A 197      14.167  18.665  56.868  1.00103.42      A
ATOM   1544  CD2 TYR A 197      15.750  16.984  58.402  1.00103.42      A
ATOM   1545  CE2 TYR A 197      15.494  18.284  58.834  1.00103.42      A
ATOM   1546  CZ  TYR A 197      14.702  19.118  58.062  1.00103.42      A
ATOM   1547  OH  TYR A 197      14.448  20.405  58.479  1.00103.42      A
ATOM   1548  C   TYR A 197      14.809  12.976  55.662  1.00 86.59      A
ATOM   1549  O   TYR A 197      15.870  12.869  55.050  1.00 86.59      A
ATOM   1550  N   THR A 198      14.011  11.940  55.910  1.00 70.57      A
ATOM   1551  CA  THR A 198      14.356  10.585  55.487  1.00 70.57      A
ATOM   1552  CB  THR A 198      15.005   9.800  56.664  1.00 81.15      A
ATOM   1553  OG1 THR A 198      16.126  10.538  57.168  1.00 81.15      A
ATOM   1554  CG2 THR A 198      15.490   8.433  56.212  1.00 81.15      A
ATOM   1555  C   THR A 198      13.107   9.836  54.999  1.00 70.57      A
ATOM   1556  O   THR A 198      12.001  10.383  55.000  1.00 70.57      A
ATOM   1557  N   LYS A 199      13.292   8.590  54.569  1.00 70.64      A
ATOM   1558  CA  LYS A 199      12.183   7.767  54.100  1.00 70.64      A
ATOM   1559  CB  LYS A 199      12.505   7.150  52.734  1.00111.90      A
ATOM   1560  CG  LYS A 199      12.700   8.164  51.617  1.00111.90      A
ATOM   1561  CD  LYS A 199      12.939   7.479  50.277  1.00111.90      A
ATOM   1562  CE  LYS A 199      13.229   8.495  49.183  1.00111.90      A
ATOM   1563  NZ  LYS A 199      12.136   9.498  49.060  1.00111.90      A

ATOM   1564  C   LYS A 199      11.894   6.656  55.108  1.00 70.64      A
ATOM   1565  O   LYS A 199      11.081   5.769  54.855  1.00 70.64      A
ATOM   1566  N   LYS A 200      12.570   6.704  56.250  1.00 62.48      A
ATOM   1567  CA  LYS A 200      12.361   5.698  57.287  1.00 62.48      A
ATOM   1568  CB  LYS A 200      13.512   5.711  58.297  1.00122.65      A
ATOM   1569  CG  LYS A 200      13.367   4.668  59.399  1.00122.65      A
ATOM   1570  CD  LYS A 200      14.522   4.716  60.391  1.00122.65      A
ATOM   1571  CE  LYS A 200      15.844   4.330  59.739  1.00122.65      A
ATOM   1572  NZ  LYS A 200      16.978   4.341  60.711  1.00122.65      A
ATOM   1573  C   LYS A 200      11.048   5.994  57.998  1.00 62.48      A
ATOM   1574  O   LYS A 200      10.874   7.062  58.580  1.00 62.48      A
ATOM   1575  N   PRO A 201      10.094   5.055  57.944  1.00 53.04      A
ATOM   1576  CD  PRO A 201      10.147   3.704  57.349  1.00 40.85      A
ATOM   1577  CA  PRO A 201       8.810   5.288  58.613  1.00 53.04      A
ATOM   1578  CB  PRO A 201       7.928   4.181  58.047  1.00 40.85      A
ATOM   1579  CG  PRO A 201       8.896   3.034  57.929  1.00 40.85      A
ATOM   1580  C   PRO A 201       8.977   5.173  60.134  1.00 53.04      A
ATOM   1581  O   PRO A 201       9.802   4.387  60.614  1.00 53.04      A
ATOM   1582  N   LYS A 202       8.210   5.955  60.886  1.00 62.83      A
ATOM   1583  CA  LYS A 202       8.305   5.890  62.335  1.00 62.83      A
ATOM   1584  CB  LYS A 202       7.868   7.220  62.958  1.00 80.05      A
ATOM   1585  CG  LYS A 202       8.905   8.314  62.716  1.00 80.05      A
ATOM   1586  CD  LYS A 202       8.771   9.507  63.650  1.00 80.05      A
ATOM   1587  CE  LYS A 202       7.669  10.458  63.216  1.00 80.05      A
ATOM   1588  NZ  LYS A 202       7.719  11.747  63.977  1.00 80.05      A
ATOM   1589  C   LYS A 202       7.501   4.714  62.881  1.00 62.83      A
ATOM   1590  O   LYS A 202       6.284   4.789  63.048  1.00 62.83      A
ATOM   1591  N   LEU A 203       8.213   3.618  63.132  1.00 68.54      A
```

FIGURE 25 CON'T

ATOM	1592	CA	LEU	A	203	7.632	2.383	63.648	1.00	68.54	A
ATOM	1593	CB	LEU	A	203	8.010	1.216	62.729	1.00	68.04	A
ATOM	1594	CG	LEU	A	203	7.748	1.390	61.230	1.00	68.04	A
ATOM	1595	CD1	LEU	A	203	8.210	0.144	60.486	1.00	68.04	A
ATOM	1596	CD2	LEU	A	203	6.260	1.637	60.984	1.00	68.04	A
ATOM	1597	C	LEU	A	203	8.136	2.090	65.072	1.00	68.54	A
ATOM	1598	O	LEU	A	203	9.148	2.642	65.507	1.00	68.54	A
ATOM	1599	N	ASP	A	204	7.423	1.219	65.783	1.00	59.83	A
ATOM	1600	CA	ASP	A	204	7.779	0.829	67.149	1.00	59.83	A
ATOM	1601	CB	ASP	A	204	7.124	1.766	68.163	1.00	106.55	A
ATOM	1602	CG	ASP	A	204	7.654	3.175	68.073	1.00	106.55	A
ATOM	1603	OD1	ASP	A	204	8.859	3.374	68.335	1.00	106.55	A
ATOM	1604	OD2	ASP	A	204	6.869	4.084	67.735	1.00	106.55	A
ATOM	1605	C	ASP	A	204	7.292	-0.589	67.393	1.00	59.83	A
ATOM	1606	O	ASP	A	204	6.095	-0.860	67.296	1.00	59.83	A
ATOM	1607	N	HIS	A	205	8.216	-1.488	67.716	1.00	74.13	A
ATOM	1608	CA	HIS	A	205	7.864	-2.883	67.957	1.00	74.13	A
ATOM	1609	CB	HIS	A	205	9.041	-3.780	67.579	1.00	98.70	A
ATOM	1610	CG	HIS	A	205	9.165	-4.006	66.106	1.00	98.70	A
ATOM	1611	CD2	HIS	A	205	9.990	-3.455	65.184	1.00	98.70	A
ATOM	1612	ND1	HIS	A	205	8.335	-4.864	65.415	1.00	98.70	A
ATOM	1613	CE1	HIS	A	205	8.644	-4.830	64.131	1.00	98.70	A
ATOM	1614	NE2	HIS	A	205	9.644	-3.983	63.964	1.00	98.70	A
ATOM	1615	C	HIS	A	205	7.391	-3.209	69.371	1.00	74.13	A
ATOM	1616	O	HIS	A	205	7.172	-4.371	69.701	1.00	74.13	A
ATOM	1617	N	ASN	A	206	7.222	-2.181	70.194	1.00	61.62	A
ATOM	1618	CA	ASN	A	206	6.756	-2.352	71.568	1.00	61.62	A
ATOM	1619	CB	ASN	A	206	6.702	-0.991	72.269	1.00	64.76	A
ATOM	1620	CG	ASN	A	206	6.416	-1.105	73.756	1.00	64.76	A
ATOM	1621	OD1	ASN	A	206	5.841	-2.091	74.222	1.00	64.76	A
ATOM	1622	ND2	ASN	A	206	6.804	-0.081	74.508	1.00	64.76	A
ATOM	1623	C	ASN	A	206	5.361	-2.993	71.594	1.00	61.62	A
ATOM	1624	O	ASN	A	206	4.366	-2.356	71.239	1.00	61.62	A
ATOM	1625	N	GLN	A	207	5.299	-4.250	72.029	1.00	53.30	A
ATOM	1626	CA	GLN	A	207	4.041	-4.994	72.114	1.00	53.30	A
ATOM	1627	CB	GLN	A	207	4.310	-6.422	72.598	1.00	74.58	A
ATOM	1628	CG	GLN	A	207	5.065	-7.282	71.602	1.00	74.58	A
ATOM	1629	CD	GLN	A	207	5.256	-8.708	72.089	1.00	74.58	A
ATOM	1630	OE1	GLN	A	207	4.338	-9.314	72.645	1.00	74.58	A
ATOM	1631	NE2	GLN	A	207	6.446	-9.256	71.866	1.00	74.58	A
ATOM	1632	C	GLN	A	207	2.992	-4.345	73.018	1.00	53.30	A
ATOM	1633	O	GLN	A	207	1.801	-4.641	72.903	1.00	53.30	A
ATOM	1634	N	GLU	A	208	3.423	-3.469	73.923	1.00	52.45	A
ATOM	1635	CA	GLU	A	208	2.474	-2.806	74.810	1.00	52.45	A
ATOM	1636	CB	GLU	A	208	3.200	-2.119	75.969	1.00	63.72	A
ATOM	1637	CG	GLU	A	208	3.997	-3.068	76.853	1.00	63.72	A
ATOM	1638	CD	GLU	A	208	3.163	-4.218	77.383	1.00	63.72	A
ATOM	1639	OE1	GLU	A	208	2.130	-3.954	78.038	1.00	63.72	A
ATOM	1640	OE2	GLU	A	208	3.544	-5.386	77.144	1.00	63.72	A
ATOM	1641	C	GLU	A	208	1.677	-1.777	74.020	1.00	52.45	A
ATOM	1642	O	GLU	A	208	0.462	-1.648	74.190	1.00	52.45	A
ATOM	1643	N	ILE	A	209	2.366	-1.037	73.154	1.00	47.68	A
ATOM	1644	CA	ILE	A	209	1.694	-0.034	72.327	1.00	47.68	A
ATOM	1645	CB	ILE	A	209	2.665	0.669	71.360	1.00	60.91	A
ATOM	1646	CG2	ILE	A	209	1.912	1.732	70.575	1.00	60.91	A
ATOM	1647	CG1	ILE	A	209	3.821	1.307	72.133	1.00	60.91	A
ATOM	1648	CD1	ILE	A	209	4.913	1.897	71.236	1.00	60.91	A

FIGURE 25 CON'T

```
ATOM   1649  C   ILE A 209      0.632  -0.740  71.488  1.00 47.68      A
ATOM   1650  O   ILE A 209     -0.519  -0.314  71.437  1.00 47.68      A
ATOM   1651  N   VAL A 210      1.034  -1.837  70.852  1.00 51.01      A
ATOM   1652  CA  VAL A 210      0.130  -2.603  70.001  1.00 51.01      A
ATOM   1653  CB  VAL A 210      0.850  -3.803  69.355  1.00 51.75      A
ATOM   1654  CG1 VAL A 210     -0.140  -4.636  68.539  1.00 51.75      A
ATOM   1655  CG2 VAL A 210      1.965  -3.305  68.464  1.00 51.75      A
ATOM   1656  C   VAL A 210     -1.082  -3.109  70.766  1.00 51.01      A
ATOM   1657  O   VAL A 210     -2.219  -2.886  70.355  1.00 51.01      A
ATOM   1658  N   LYS A 211     -0.841  -3.786  71.882  1.00 51.09      A
ATOM   1659  CA  LYS A 211     -1.935  -4.312  72.692  1.00 51.09      A
ATOM   1660  CB  LYS A 211     -1.381  -5.026  73.930  1.00107.12      A
ATOM   1661  CG  LYS A 211     -2.448  -5.719  74.768  1.00107.12      A
ATOM   1662  CD  LYS A 211     -3.215  -6.751  73.945  1.00107.12      A
ATOM   1663  CE  LYS A 211     -4.386  -7.338  74.720  1.00107.12      A
ATOM   1664  NZ  LYS A 211     -5.135  -8.342  73.912  1.00107.12      A
ATOM   1665  C   LYS A 211     -2.894  -3.200  73.119  1.00 51.09      A
ATOM   1666  O   LYS A 211     -4.116  -3.309  72.951  1.00 51.09      A
ATOM   1667  N   TYR A 212     -2.332  -2.120  73.652  1.00 49.34      A
ATOM   1668  CA  TYR A 212     -3.137  -0.999  74.116  1.00 49.34      A
ATOM   1669  CB  TYR A 212     -2.250   0.135  74.633  1.00 56.43      A
ATOM   1670  CG  TYR A 212     -3.056   1.308  75.153  1.00 56.43      A
ATOM   1671  CD1 TYR A 212     -3.607   1.293  76.443  1.00 56.43      A
ATOM   1672  CE1 TYR A 212     -4.403   2.349  76.906  1.00 56.43      A
ATOM   1673  CD2 TYR A 212     -3.318   2.412  74.339  1.00 56.43      A
ATOM   1674  CE2 TYR A 212     -4.110   3.470  74.790  1.00 56.43      A
ATOM   1675  CZ  TYR A 212     -4.651   3.432  76.072  1.00 56.43      A
ATOM   1676  OH  TYR A 212     -5.451   4.472  76.498  1.00 56.43      A
ATOM   1677  C   TYR A 212     -4.078  -0.430  73.063  1.00 49.34      A
ATOM   1678  O   TYR A 212     -5.290  -0.351  73.283  1.00 49.34      A
ATOM   1679  N   TRP A 213     -3.530  -0.015  71.922  1.00 53.75      A
ATOM   1680  CA  TRP A 213     -4.372   0.566  70.883  1.00 53.75      A
ATOM   1681  CB  TRP A 213     -3.507   1.327  69.876  1.00 45.29      A
ATOM   1682  CG  TRP A 213     -2.937   2.567  70.517  1.00 45.29      A
ATOM   1683  CD2 TRP A 213     -3.680   3.696  71.002  1.00 45.29      A
ATOM   1684  CE2 TRP A 213     -2.751   4.594  71.572  1.00 45.29      A
ATOM   1685  CE3 TRP A 213     -5.042   4.034  71.011  1.00 45.29      A
ATOM   1686  CD1 TRP A 213     -1.624   2.820  70.805  1.00 45.29      A
ATOM   1687  NE1 TRP A 213     -1.506   4.035  71.440  1.00 45.29      A
ATOM   1688  CZ2 TRP A 213     -3.138   5.811  72.146  1.00 45.29      A
ATOM   1689  CZ3 TRP A 213     -5.429   5.248  71.582  1.00 45.29      A
ATOM   1690  CH2 TRP A 213     -4.476   6.121  72.141  1.00 45.29      A
ATOM   1691  C   TRP A 213     -5.309  -0.427  70.204  1.00 53.75      A

ATOM   1692  O   TRP A 213     -6.370  -0.042  69.710  1.00 53.75      A
ATOM   1693  N   TYR A 214     -4.938  -1.703  70.191  1.00 46.49      A
ATOM   1694  CA  TYR A 214     -5.824  -2.713  69.614  1.00 46.49      A
ATOM   1695  CB  TYR A 214     -5.120  -4.067  69.522  1.00 46.14      A
ATOM   1696  CG  TYR A 214     -6.029  -5.212  69.116  1.00 46.14      A
ATOM   1697  CD1 TYR A 214     -5.952  -5.772  67.843  1.00 46.14      A
ATOM   1698  CE1 TYR A 214     -6.763  -6.850  67.478  1.00 46.14      A
ATOM   1699  CD2 TYR A 214     -6.950  -5.756  70.020  1.00 46.14      A
ATOM   1700  CE2 TYR A 214     -7.768  -6.830  69.666  1.00 46.14      A
ATOM   1701  CZ  TYR A 214     -7.666  -7.376  68.393  1.00 46.14      A
ATOM   1702  OH  TYR A 214     -8.447  -8.462  68.046  1.00 46.14      A
ATOM   1703  C   TYR A 214     -7.023  -2.823  70.562  1.00 46.49      A
ATOM   1704  O   TYR A 214     -8.180  -2.791  70.135  1.00 46.49      A
```

FIGURE 25 CON'T

```
ATOM   1705  N   ASN A 215      -6.737  -2.954  71.857  1.00 53.54      A
ATOM   1706  CA  ASN A 215      -7.797  -3.057  72.854  1.00 53.54      A
ATOM   1707  CB  ASN A 215      -7.199  -3.338  74.237  1.00 73.57      A
ATOM   1708  CG  ASN A 215      -8.211  -3.167  75.357  1.00 73.57      A
ATOM   1709  OD1 ASN A 215      -8.447  -2.052  75.836  1.00 73.57      A
ATOM   1710  ND2 ASN A 215      -8.828  -4.272  75.770  1.00 73.57      A
ATOM   1711  C   ASN A 215      -8.627  -1.778  72.889  1.00 53.54      A
ATOM   1712  O   ASN A 215      -9.838  -1.813  73.117  1.00 53.54      A
ATOM   1713  N   TYR A 216      -7.970  -0.650  72.657  1.00 55.91      A
ATOM   1714  CA  TYR A 216      -8.656   0.635  72.650  1.00 55.91      A
ATOM   1715  CB  TYR A 216      -7.697   1.746  72.236  1.00 71.73      A
ATOM   1716  CG  TYR A 216      -8.340   3.111  72.213  1.00 71.73      A
ATOM   1717  CD1 TYR A 216      -8.384   3.901  73.363  1.00 71.73      A
ATOM   1718  CE1 TYR A 216      -8.981   5.161  73.349  1.00 71.73      A
ATOM   1719  CD2 TYR A 216      -8.915   3.612  71.045  1.00 71.73      A
ATOM   1720  CE2 TYR A 216      -9.519   4.870  71.018  1.00 71.73      A
ATOM   1721  CZ  TYR A 216      -9.547   5.640  72.174  1.00 71.73      A
ATOM   1722  OH  TYR A 216     -10.130   6.889  72.158  1.00 71.73      A
ATOM   1723  C   TYR A 216      -9.866   0.652  71.705  1.00 55.91      A
ATOM   1724  O   TYR A 216     -10.932   1.155  72.068  1.00 55.91      A
ATOM   1725  N   HIS A 217      -9.703   0.124  70.492  1.00 53.08      A
ATOM   1726  CA  HIS A 217     -10.810   0.116  69.533  1.00 53.08      A
ATOM   1727  CB  HIS A 217     -10.401  -0.505  68.187  1.00 46.99      A
ATOM   1728  CG  HIS A 217      -9.496   0.356  67.368  1.00 46.99      A
ATOM   1729  CD2 HIS A 217      -9.754   1.180  66.324  1.00 46.99      A
ATOM   1730  ND1 HIS A 217      -8.143   0.453  67.608  1.00 46.99      A
ATOM   1731  CE1 HIS A 217      -7.606   1.300  66.747  1.00 46.99      A
ATOM   1732  NE2 HIS A 217      -8.561   1.755  65.957  1.00 46.99      A
ATOM   1733  C   HIS A 217     -12.006  -0.653  70.064  1.00 53.08      A
ATOM   1734  O   HIS A 217     -13.141  -0.198  69.962  1.00 53.08      A
ATOM   1735  N   ILE A 218     -11.748  -1.827  70.620  1.00 54.18      A
ATOM   1736  CA  ILE A 218     -12.822  -2.650  71.145  1.00 54.18      A
ATOM   1737  CB  ILE A 218     -12.283  -4.022  71.561  1.00 55.73      A
ATOM   1738  CG2 ILE A 218     -13.388  -4.843  72.200  1.00 55.73      A
ATOM   1739  CG1 ILE A 218     -11.712  -4.726  70.322  1.00 55.73      A
ATOM   1740  CD1 ILE A 218     -11.023  -6.035  70.598  1.00 55.73      A
ATOM   1741  C   ILE A 218     -13.549  -1.978  72.310  1.00 54.18      A
ATOM   1742  O   ILE A 218     -14.770  -1.846  72.284  1.00 54.18      A
ATOM   1743  N   GLU A 219     -12.800  -1.533  73.314  1.00 75.71      A
ATOM   1744  CA  GLU A 219     -13.391  -0.870  74.477  1.00 75.71      A
ATOM   1745  CB  GLU A 219     -12.291  -0.406  75.440  1.00 74.86      A
ATOM   1746  CG  GLU A 219     -12.088  -1.299  76.651  1.00 74.86      A
ATOM   1747  CD  GLU A 219     -13.337  -1.411  77.510  1.00 74.86      A
ATOM   1748  OE1 GLU A 219     -13.868  -0.365  77.939  1.00 74.86      A
ATOM   1749  OE2 GLU A 219     -13.786  -2.551  77.755  1.00 74.86      A
ATOM   1750  C   GLU A 219     -14.259   0.338  74.125  1.00 75.71      A
ATOM   1751  O   GLU A 219     -15.378   0.481  74.620  1.00 75.71      A
ATOM   1752  N   ARG A 220     -13.730   1.206  73.271  1.00 74.22      A
ATOM   1753  CA  ARG A 220     -14.419   2.427  72.872  1.00 74.22      A
ATOM   1754  CB  ARG A 220     -13.365   3.489  72.525  1.00 98.22      A
ATOM   1755  CG  ARG A 220     -13.686   4.347  71.317  1.00 98.22      A
ATOM   1756  CD  ARG A 220     -14.576   5.526  71.649  1.00 98.22      A
ATOM   1757  NE  ARG A 220     -13.799   6.686  72.076  1.00 98.22      A
ATOM   1758  CZ  ARG A 220     -14.275   7.926  72.113  1.00 98.22      A
ATOM   1759  NH1 ARG A 220     -15.527   8.169  71.747  1.00 98.22      A
ATOM   1760  NH2 ARG A 220     -13.498   8.926  72.508  1.00 98.22      A
ATOM   1761  C   ARG A 220     -15.452   2.316  71.738  1.00 74.22      A
```

FIGURE 25 CON'T

```
ATOM   1762  O   ARG A 220     -16.399   3.102  71.691  1.00 74.22      A
ATOM   1763  N   TYR A 221     -15.299   1.349  70.840  1.00 70.93      A
ATOM   1764  CA  TYR A 221     -16.241   1.249  69.725  1.00 70.93      A
ATOM   1765  CB  TYR A 221     -15.500   1.446  68.401  1.00 67.88      A
ATOM   1766  CG  TYR A 221     -14.785   2.770  68.281  1.00 67.88      A
ATOM   1767  CD1 TYR A 221     -15.483   3.975  68.377  1.00 67.88      A
ATOM   1768  CE1 TYR A 221     -14.828   5.200  68.244  1.00 67.88      A
ATOM   1769  CD2 TYR A 221     -13.412   2.820  68.051  1.00 67.88      A
ATOM   1770  CE2 TYR A 221     -12.748   4.033  67.919  1.00 67.88      A
ATOM   1771  CZ  TYR A 221     -13.460   5.219  68.015  1.00 67.88      A
ATOM   1772  OH  TYR A 221     -12.797   6.417  67.882  1.00 67.88      A
ATOM   1773  C   TYR A 221     -17.115   0.008  69.601  1.00 70.93      A
ATOM   1774  O   TYR A 221     -18.255   0.109  69.154  1.00 70.93      A
ATOM   1775  N   TRP A 222     -16.599  -1.158  69.972  1.00 62.80      A
ATOM   1776  CA  TRP A 222     -17.383  -2.384  69.846  1.00 62.80      A
ATOM   1777  CB  TRP A 222     -16.775  -3.286  68.767  1.00 91.59      A
ATOM   1778  CG  TRP A 222     -16.252  -2.534  67.584  1.00 91.59      A
ATOM   1779  CD2 TRP A 222     -17.017  -2.014  66.490  1.00 91.59      A
ATOM   1780  CE2 TRP A 222     -16.119  -1.333  65.640  1.00 91.59      A
ATOM   1781  CE3 TRP A 222     -18.375  -2.056  66.146  1.00 91.59      A
ATOM   1782  CD1 TRP A 222     -14.959  -2.160  67.359  1.00 91.59      A
ATOM   1783  NE1 TRP A 222     -14.870  -1.438  66.194  1.00 91.59      A
ATOM   1784  CZ2 TRP A 222     -16.534  -0.696  64.466  1.00 91.59      A
ATOM   1785  CZ3 TRP A 222     -18.789  -1.423  64.979  1.00 91.59      A
ATOM   1786  CH2 TRP A 222     -17.869  -0.752  64.153  1.00 91.59      A
ATOM   1787  C   TRP A 222     -17.468  -3.154  71.153  1.00 62.80      A
ATOM   1788  O   TRP A 222     -17.245  -4.366  71.178  1.00 62.80      A
ATOM   1789  N   ASN A 223     -17.813  -2.452  72.228  1.00 84.04      A
ATOM   1790  CA  ASN A 223     -17.910  -3.055  73.555  1.00 84.04      A
ATOM   1791  CB  ASN A 223     -17.825  -1.958  74.623  1.00128.47      A
ATOM   1792  CG  ASN A 223     -17.529  -2.507  76.007  1.00128.47      A
ATOM   1793  OD1 ASN A 223     -18.229  -3.387  76.504  1.00128.47      A
ATOM   1794  ND2 ASN A 223     -16.486  -1.982  76.638  1.00128.47      A
ATOM   1795  C   ASN A 223     -19.182  -3.882  73.773  1.00 84.04      A
ATOM   1796  O   ASN A 223     -19.931  -3.642  74.717  1.00 84.04      A
ATOM   1797  N   THR A 224     -19.430  -4.849  72.898  1.00 66.05      A
ATOM   1798  CA  THR A 224     -20.603  -5.707  73.029  1.00 66.05      A
ATOM   1799  CB  THR A 224     -21.816  -5.168  72.235  1.00 84.17      A
ATOM   1800  OG1 THR A 224     -21.571  -5.309  70.832  1.00 84.17      A
ATOM   1801  CG2 THR A 224     -22.063  -3.702  72.555  1.00 84.17      A
ATOM   1802  C   THR A 224     -20.251  -7.087  72.486  1.00 66.05      A
ATOM   1803  O   THR A 224     -19.498  -7.211  71.520  1.00 66.05      A
ATOM   1804  N   PRO A 225     -20.785  -8.148  73.105  1.00 84.76      A
ATOM   1805  CD  PRO A 225     -21.668  -8.182  74.286  1.00 62.62      A
ATOM   1806  CA  PRO A 225     -20.486  -9.502  72.635  1.00 84.76      A
ATOM   1807  CB  PRO A 225     -21.483 -10.355  73.412  1.00 62.62      A
ATOM   1808  CG  PRO A 225     -21.568  -9.626  74.723  1.00 62.62      A
ATOM   1809  C   PRO A 225     -20.623  -9.668  71.116  1.00 84.76      A
ATOM   1810  O   PRO A 225     -19.780 -10.292  70.469  1.00 84.76      A
ATOM   1811  N   GLU A 226     -21.682  -9.099  70.550  1.00 72.64      A
ATOM   1812  CA  GLU A 226     -21.916  -9.211  69.117  1.00 72.64      A
ATOM   1813  CB  GLU A 226     -23.335  -8.747  68.782  1.00147.05      A
ATOM   1814  CG  GLU A 226     -24.414  -9.534  69.507  1.00147.05      A
ATOM   1815  CD  GLU A 226     -25.810  -9.198  69.023  1.00147.05      A
ATOM   1816  OE1 GLU A 226     -26.196  -8.012  69.085  1.00147.05      A
ATOM   1817  OE2 GLU A 226     -26.523 -10.125  68.583  1.00147.05      A
ATOM   1818  C   GLU A 226     -20.898  -8.420  68.303  1.00 72.64      A
```

FIGURE 25 CON'T

```
ATOM   1819  O   GLU A 226     -20.334  -8.931  67.333  1.00 72.64      A

ATOM   1820  N   ALA A 227     -20.660  -7.173  68.694  1.00 77.94      A
ATOM   1821  CA  ALA A 227     -19.699  -6.344  67.979  1.00 77.94      A
ATOM   1822  CB  ALA A 227     -19.760  -4.910  68.490  1.00 58.35      A
ATOM   1823  C   ALA A 227     -18.288  -6.914  68.142  1.00 77.94      A
ATOM   1824  O   ALA A 227     -17.491  -6.896  67.203  1.00 77.94      A
ATOM   1825  N   LYS A 228     -17.996  -7.430  69.335  1.00 58.30      A
ATOM   1826  CA  LYS A 228     -16.694  -8.016  69.635  1.00 58.30      A
ATOM   1827  CB  LYS A 228     -16.630  -8.483  71.090  1.00 76.00      A
ATOM   1828  CG  LYS A 228     -16.501  -7.399  72.136  1.00 76.00      A
ATOM   1829  CD  LYS A 228     -16.430  -8.034  73.520  1.00 76.00      A
ATOM   1830  CE  LYS A 228     -16.311  -6.996  74.620  1.00 76.00      A
ATOM   1831  NZ  LYS A 228     -16.287  -7.636  75.966  1.00 76.00      A
ATOM   1832  C   LYS A 228     -16.431  -9.220  68.749  1.00 58.30      A
ATOM   1833  O   LYS A 228     -15.311  -9.432  68.280  1.00 58.30      A
ATOM   1834  N   LEU A 229     -17.469 -10.022  68.545  1.00 61.22      A
ATOM   1835  CA  LEU A 229     -17.350 -11.218  67.731  1.00 61.22      A
ATOM   1836  CB  LEU A 229     -18.655 -12.015  67.770  1.00 70.56      A
ATOM   1837  CG  LEU A 229     -18.560 -13.534  67.604  1.00 70.56      A
ATOM   1838  CD1 LEU A 229     -19.956 -14.073  67.339  1.00 70.56      A
ATOM   1839  CD2 LEU A 229     -17.628 -13.907  66.466  1.00 70.56      A
ATOM   1840  C   LEU A 229     -17.035 -10.829  66.292  1.00 61.22      A
ATOM   1841  O   LEU A 229     -16.155 -11.413  65.663  1.00 61.22      A
ATOM   1842  N   GLU A 230     -17.759  -9.841  65.774  1.00 65.81      A
ATOM   1843  CA  GLU A 230     -17.542  -9.400  64.405  1.00 65.81      A
ATOM   1844  CB  GLU A 230     -18.571  -8.339  64.012  1.00111.18      A
ATOM   1845  CG  GLU A 230     -18.604  -8.063  62.517  1.00111.18      A
ATOM   1846  CD  GLU A 230     -19.660  -7.048  62.128  1.00111.18      A
ATOM   1847  OE1 GLU A 230     -20.849  -7.269  62.446  1.00111.18      A
ATOM   1848  OE2 GLU A 230     -19.300  -6.030  61.500  1.00111.18      A
ATOM   1849  C   GLU A 230     -16.134  -8.839  64.263  1.00 65.81      A
ATOM   1850  O   GLU A 230     -15.428  -9.133  63.293  1.00 65.81      A
ATOM   1851  N   PHE A 231     -15.726  -8.039  65.243  1.00 56.50      A
ATOM   1852  CA  PHE A 231     -14.399  -7.446  65.228  1.00 56.50      A
ATOM   1853  CB  PHE A 231     -14.155  -6.654  66.509  1.00 59.08      A
ATOM   1854  CG  PHE A 231     -12.802  -6.010  66.570  1.00 59.08      A
ATOM   1855  CD1 PHE A 231     -12.615  -4.712  66.117  1.00 59.08      A
ATOM   1856  CD2 PHE A 231     -11.707  -6.714  67.065  1.00 59.08      A
ATOM   1857  CE1 PHE A 231     -11.355  -4.121  66.157  1.00 59.08      A
ATOM   1858  CE2 PHE A 231     -10.447  -6.132  67.107  1.00 59.08      A
ATOM   1859  CZ  PHE A 231     -10.270  -4.834  66.654  1.00 59.08      A
ATOM   1860  C   PHE A 231     -13.350  -8.544  65.097  1.00 56.50      A
ATOM   1861  O   PHE A 231     -12.457  -8.467  64.247  1.00 56.50      A
ATOM   1862  N   TYR A 232     -13.456  -9.572  65.933  1.00 57.07      A
ATOM   1863  CA  TYR A 232     -12.497 -10.677  65.879  1.00 57.07      A
ATOM   1864  CB  TYR A 232     -12.660 -11.578  67.106  1.00 68.47      A
ATOM   1865  CG  TYR A 232     -11.837 -11.108  68.282  1.00 68.47      A
ATOM   1866  CD1 TYR A 232     -10.530 -11.550  68.458  1.00 68.47      A
ATOM   1867  CE1 TYR A 232      -9.748 -11.085  69.507  1.00 68.47      A
ATOM   1868  CD2 TYR A 232     -12.348 -10.183  69.192  1.00 68.47      A
ATOM   1869  CE2 TYR A 232     -11.575  -9.709  70.246  1.00 68.47      A
ATOM   1870  CZ  TYR A 232     -10.274 -10.165  70.398  1.00 68.47      A
ATOM   1871  OH  TYR A 232      -9.497  -9.695  71.437  1.00 68.47      A
ATOM   1872  C   TYR A 232     -12.620 -11.491  64.593  1.00 57.07      A
ATOM   1873  O   TYR A 232     -11.637 -12.060  64.109  1.00 57.07      A
ATOM   1874  N   ARG A 233     -13.823 -11.545  64.035  1.00 65.42      A
```

FIGURE 25 CON'T

```
ATOM   1875  CA  ARG A 233     -14.023 -12.274  62.787  1.00 65.42      A
ATOM   1876  CB  ARG A 233     -15.513 -12.396  62.452  1.00 90.05      A
ATOM   1877  CG  ARG A 233     -16.302 -13.367  63.310  1.00 90.05      A
ATOM   1878  CD  ARG A 233     -17.130 -14.284  62.422  1.00 90.05      A
ATOM   1879  NE  ARG A 233     -18.264 -14.885  63.118  1.00 90.05      A
ATOM   1880  CZ  ARG A 233     -19.316 -14.203  63.561  1.00 90.05      A
ATOM   1881  NH1 ARG A 233     -19.383 -12.888  63.385  1.00 90.05      A
ATOM   1882  NH2 ARG A 233     -20.308 -14.837  64.170  1.00 90.05      A
ATOM   1883  C   ARG A 233     -13.329 -11.515  61.658  1.00 65.42      A
ATOM   1884  O   ARG A 233     -12.673 -12.109  60.804  1.00 65.42      A
ATOM   1885  N   LYS A 234     -13.475 -10.194  61.677  1.00 66.11      A
ATOM   1886  CA  LYS A 234     -12.899  -9.327  60.654  1.00 66.11      A
ATOM   1887  CB  LYS A 234     -13.600  -7.964  60.689  1.00 82.51      A
ATOM   1888  CG  LYS A 234     -13.204  -7.020  59.569  1.00 82.51      A
ATOM   1889  CD  LYS A 234     -14.013  -5.732  59.621  1.00 82.51      A
ATOM   1890  CE  LYS A 234     -13.630  -4.794  58.484  1.00 82.51      A
ATOM   1891  NZ  LYS A 234     -14.323  -3.474  58.565  1.00 82.51      A
ATOM   1892  C   LYS A 234     -11.388  -9.128  60.761  1.00 66.11      A
ATOM   1893  O   LYS A 234     -10.661  -9.295  59.777  1.00 66.11      A
ATOM   1894  N   PHE A 235     -10.908  -8.790  61.953  1.00 53.14      A
ATOM   1895  CA  PHE A 235      -9.483  -8.541  62.132  1.00 53.14      A
ATOM   1896  CB  PHE A 235      -9.307  -7.248  62.911  1.00 56.44      A
ATOM   1897  CG  PHE A 235     -10.017  -6.085  62.295  1.00 56.44      A
ATOM   1898  CD1 PHE A 235      -9.577  -5.548  61.088  1.00 56.44      A
ATOM   1899  CD2 PHE A 235     -11.138  -5.535  62.910  1.00 56.44      A
ATOM   1900  CE1 PHE A 235     -10.242  -4.477  60.501  1.00 56.44      A
ATOM   1901  CE2 PHE A 235     -11.814  -4.465  62.333  1.00 56.44      A
ATOM   1902  CZ  PHE A 235     -11.364  -3.933  61.124  1.00 56.44      A
ATOM   1903  C   PHE A 235      -8.679  -9.651  62.792  1.00 53.14      A
ATOM   1904  O   PHE A 235      -7.457  -9.729  62.615  1.00 53.14      A
ATOM   1905  N   GLY A 236      -9.355 -10.514  63.542  1.00 55.50      A
ATOM   1906  CA  GLY A 236      -8.654 -11.589  64.223  1.00 55.50      A
ATOM   1907  C   GLY A 236      -7.992 -11.062  65.487  1.00 55.50      A
ATOM   1908  O   GLY A 236      -7.978  -9.855  65.728  1.00 55.50      A
ATOM   1909  N   GLN A 237      -7.438 -11.963  66.291  1.00 59.58      A
ATOM   1910  CA  GLN A 237      -6.780 -11.571  67.529  1.00 59.58      A
ATOM   1911  CB  GLN A 237      -6.314 -12.807  68.307  1.00109.64      A
ATOM   1912  CG  GLN A 237      -7.444 -13.720  68.767  1.00109.64      A
ATOM   1913  CD  GLN A 237      -6.986 -14.759  69.781  1.00109.64      A
ATOM   1914  OE1 GLN A 237      -6.077 -15.546  69.517  1.00109.64      A
ATOM   1915  NE2 GLN A 237      -7.620 -14.763  70.949  1.00109.64      A
ATOM   1916  C   GLN A 237      -5.592 -10.677  67.237  1.00 59.58      A
ATOM   1917  O   GLN A 237      -5.050 -10.701  66.139  1.00 59.58      A
ATOM   1918  N   VAL A 238      -5.200  -9.889  68.232  1.00 56.69      A
ATOM   1919  CA  VAL A 238      -4.069  -8.980  68.105  1.00 56.69      A
ATOM   1920  CB  VAL A 238      -3.695  -8.327  69.448  1.00 79.40      A
ATOM   1921  CG1 VAL A 238      -2.951  -7.025  69.204  1.00 79.40      A
ATOM   1922  CG2 VAL A 238      -4.919  -8.122  70.287  1.00 79.40      A
ATOM   1923  C   VAL A 238      -2.837  -9.747  67.670  1.00 56.69      A
ATOM   1924  O   VAL A 238      -2.550 -10.824  68.196  1.00 56.69      A
ATOM   1925  N   ASP A 239      -2.101  -9.190  66.719  1.00 49.95      A
ATOM   1926  CA  ASP A 239      -0.878  -9.826  66.265  1.00 49.95      A
ATOM   1927  CB  ASP A 239      -0.792  -9.814  64.737  1.00 59.63      A
ATOM   1928  CG  ASP A 239       0.354 -10.654  64.220  1.00 59.63      A
ATOM   1929  OD1 ASP A 239       0.206 -11.260  63.139  1.00 59.63      A
ATOM   1930  OD2 ASP A 239       1.406 -10.708  64.889  1.00 59.63      A
ATOM   1931  C   ASP A 239       0.226  -8.987  66.891  1.00 49.95      A
```

FIGURE 25 CON'T

```
ATOM   1932  O   ASP A 239       0.419  -7.826  66.531  1.00 49.95      A
ATOM   1933  N   LEU A 240       0.930  -9.579  67.850  1.00 56.76      A
ATOM   1934  CA  LEU A 240       1.983  -8.887  68.576  1.00 56.76      A
ATOM   1935  CB  LEU A 240       2.270  -9.622  69.886  1.00 64.97      A
ATOM   1936  CG  LEU A 240       1.064  -9.867  70.796  1.00 64.97      A
ATOM   1937  CD1 LEU A 240       1.507 -10.675  72.015  1.00 64.97      A
ATOM   1938  CD2 LEU A 240       0.445  -8.537  71.212  1.00 64.97      A
ATOM   1939  C   LEU A 240       3.274  -8.723  67.793  1.00 56.76      A
ATOM   1940  O   LEU A 240       4.166  -7.992  68.218  1.00 56.76      A
ATOM   1941  N   LYS A 241       3.379  -9.396  66.652  1.00 60.83      A
ATOM   1942  CA  LYS A 241       4.586  -9.289  65.843  1.00 60.83      A
ATOM   1943  CB  LYS A 241       4.756 -10.538  64.976  1.00100.72      A
ATOM   1944  CG  LYS A 241       5.042 -11.793  65.787  1.00100.72      A
ATOM   1945  CD  LYS A 241       5.175 -13.021  64.907  1.00100.72      A
ATOM   1946  CE  LYS A 241       5.448 -14.258  65.747  1.00100.72      A
ATOM   1947  NZ  LYS A 241       5.548 -15.489  64.917  1.00100.72      A

ATOM   1948  C   LYS A 241       4.594  -8.038  64.969  1.00 60.83      A
ATOM   1949  O   LYS A 241       5.624  -7.681  64.401  1.00 60.83      A
ATOM   1950  N   GLN A 242       3.449  -7.367  64.879  1.00 55.00      A
ATOM   1951  CA  GLN A 242       3.334  -6.157  64.069  1.00 55.00      A
ATOM   1952  CB  GLN A 242       1.876  -5.923  63.644  1.00 46.50      A
ATOM   1953  CG  GLN A 242       1.020  -5.292  64.737  1.00 46.50      A
ATOM   1954  CD  GLN A 242      -0.455  -5.192  64.380  1.00 46.50      A
ATOM   1955  OE1 GLN A 242      -0.872  -4.309  63.612  1.00 46.50      A
ATOM   1956  NE2 GLN A 242      -1.258  -6.097  64.936  1.00 46.50      A
ATOM   1957  C   GLN A 242       3.805  -4.934  64.841  1.00 55.00      A
ATOM   1958  O   GLN A 242       3.556  -4.809  66.038  1.00 55.00      A
ATOM   1959  N   PRO A 243       4.514  -4.021  64.170  1.00 58.47      A
ATOM   1960  CD  PRO A 243       5.203  -4.174  62.876  1.00 59.24      A
ATOM   1961  CA  PRO A 243       4.973  -2.818  64.866  1.00 58.47      A
ATOM   1962  CB  PRO A 243       6.197  -2.403  64.058  1.00 59.24      A
ATOM   1963  CG  PRO A 243       5.809  -2.802  62.670  1.00 59.24      A
ATOM   1964  C   PRO A 243       3.855  -1.779  64.787  1.00 58.47      A
ATOM   1965  O   PRO A 243       2.936  -1.922  63.979  1.00 58.47      A
ATOM   1966  N   ALA A 244       3.924  -0.749  65.623  1.00 48.59      A
ATOM   1967  CA  ALA A 244       2.917   0.302  65.603  1.00 48.59      A
ATOM   1968  CB  ALA A 244       2.690   0.851  67.008  1.00 34.86      A
ATOM   1969  C   ALA A 244       3.401   1.414  64.669  1.00 48.59      A
ATOM   1970  O   ALA A 244       4.594   1.695  64.599  1.00 48.59      A
ATOM   1971  N   ILE A 245       2.468   2.035  63.955  1.00 51.52      A
ATOM   1972  CA  ILE A 245       2.796   3.103  63.012  1.00 51.52      A
ATOM   1973  CB  ILE A 245       2.026   2.907  61.675  1.00 46.20      A
ATOM   1974  CG2 ILE A 245       2.248   4.090  60.748  1.00 46.20      A
ATOM   1975  CG1 ILE A 245       2.477   1.602  61.009  1.00 46.20      A
ATOM   1976  CD1 ILE A 245       1.664   1.232  59.792  1.00 46.20      A
ATOM   1977  C   ILE A 245       2.453   4.473  63.578  1.00 51.52      A
ATOM   1978  O   ILE A 245       1.289   4.767  63.843  1.00 51.52      A
ATOM   1979  N   LEU A 246       3.462   5.315  63.766  1.00 48.33      A
ATOM   1980  CA  LEU A 246       3.196   6.649  64.285  1.00 48.33      A
ATOM   1981  CB  LEU A 246       4.468   7.273  64.859  1.00 54.70      A
ATOM   1982  CG  LEU A 246       4.190   8.580  65.601  1.00 54.70      A
ATOM   1983  CD1 LEU A 246       3.261   8.307  66.780  1.00 54.70      A
ATOM   1984  CD2 LEU A 246       5.498   9.199  66.073  1.00 54.70      A
ATOM   1985  C   LEU A 246       2.677   7.490  63.122  1.00 48.33      A
ATOM   1986  O   LEU A 246       3.335   7.600  62.083  1.00 48.33      A
ATOM   1987  N   ALA A 247       1.500   8.080  63.287  1.00 60.06      A
```

FIGURE 25 CON'T

ATOM	1988	CA	ALA	A	247	0.911	8.869	62.214	1.00	60.06	A
ATOM	1989	CB	ALA	A	247	-0.029	7.986	61.383	1.00	51.98	A
ATOM	1990	C	ALA	A	247	0.155	10.078	62.723	1.00	60.06	A
ATOM	1991	O	ALA	A	247	0.149	10.370	63.918	1.00	60.06	A
ATOM	1992	N	LYS	A	248	-0.484	10.782	61.796	1.00	56.31	A
ATOM	1993	CA	LYS	A	248	-1.265	11.960	62.126	1.00	56.31	A
ATOM	1994	CB	LYS	A	248	-0.407	13.221	61.984	1.00	104.99	A
ATOM	1995	CG	LYS	A	248	0.449	13.253	60.731	1.00	104.99	A
ATOM	1996	CD	LYS	A	248	1.273	14.536	60.631	1.00	104.99	A
ATOM	1997	CE	LYS	A	248	2.226	14.719	61.814	1.00	104.99	A
ATOM	1998	NZ	LYS	A	248	1.530	15.068	63.088	1.00	104.99	A
ATOM	1999	C	LYS	A	248	-2.482	12.039	61.216	1.00	56.31	A
ATOM	2000	O	LYS	A	248	-2.551	11.363	60.185	1.00	56.31	A
ATOM	2001	N	PHE	A	249	-3.446	12.859	61.610	1.00	63.28	A
ATOM	2002	CA	PHE	A	249	-4.661	13.030	60.838	1.00	63.28	A
ATOM	2003	CB	PHE	A	249	-5.592	14.004	61.557	1.00	78.87	A
ATOM	2004	CG	PHE	A	249	-6.051	13.511	62.897	1.00	78.87	A
ATOM	2005	CD1	PHE	A	249	-6.909	12.420	62.992	1.00	78.87	A
ATOM	2006	CD2	PHE	A	249	-5.602	14.115	64.065	1.00	78.87	A
ATOM	2007	CE1	PHE	A	249	-7.313	11.935	64.235	1.00	78.87	A
ATOM	2008	CE2	PHE	A	249	-5.999	13.639	65.314	1.00	78.87	A
ATOM	2009	CZ	PHE	A	249	-6.855	12.547	65.399	1.00	78.87	A
ATOM	2010	C	PHE	A	249	-4.350	13.534	59.436	1.00	63.28	A
ATOM	2011	O	PHE	A	249	-3.432	14.345	59.236	1.00	63.28	A
ATOM	2012	N	ALA	A	250	-5.113	13.039	58.465	1.00	68.59	A
ATOM	2013	CA	ALA	A	250	-4.935	13.438	57.078	1.00	68.59	A
ATOM	2014	CB	ALA	A	250	-5.461	12.346	56.153	1.00	55.71	A
ATOM	2015	C	ALA	A	250	-5.659	14.756	56.799	1.00	68.59	A
ATOM	2016	O	ALA	A	250	-5.209	15.562	55.982	1.00	68.59	A
ATOM	2017	N	SER	A	251	-6.772	14.972	57.493	1.00	76.45	A
ATOM	2018	CA	SER	A	251	-7.582	16.175	57.317	1.00	76.45	A
ATOM	2019	CB	SER	A	251	-8.890	16.032	58.099	1.00	150.67	A
ATOM	2020	OG	SER	A	251	-8.635	15.831	59.480	1.00	150.67	A
ATOM	2021	C	SER	A	251	-6.890	17.480	57.722	1.00	76.45	A
ATOM	2022	O	SER	A	251	-5.672	17.616	57.598	1.00	76.45	A
ATOM	2023	N	LYS	A	252	-7.688	18.432	58.204	1.00	116.94	A
ATOM	2024	CA	LYS	A	252	-7.206	19.746	58.626	1.00	116.94	A
ATOM	2025	CB	LYS	A	252	-5.914	19.623	59.445	1.00	124.94	A
ATOM	2026	CG	LYS	A	252	-6.066	18.863	60.753	1.00	124.94	A
ATOM	2027	CD	LYS	A	252	-4.724	18.721	61.457	1.00	124.94	A
ATOM	2028	CE	LYS	A	252	-4.853	17.950	62.763	1.00	124.94	A
ATOM	2029	NZ	LYS	A	252	-5.732	18.647	63.743	1.00	124.94	A
ATOM	2030	C	LYS	A	252	-6.957	20.629	57.409	1.00	116.94	A
ATOM	2031	O	LYS	A	252	-7.464	20.356	56.320	1.00	116.94	A
ATOM	2032	N	ASN	A	258	1.361	17.852	65.655	1.00	150.47	A
ATOM	2033	CA	ASN	A	258	0.210	18.540	66.229	1.00	150.47	A
ATOM	2034	CB	ASN	A	258	-0.659	19.139	65.116	1.00	149.86	A
ATOM	2035	CG	ASN	A	258	-1.774	20.029	65.651	1.00	149.86	A
ATOM	2036	OD1	ASN	A	258	-2.656	20.452	64.903	1.00	149.86	A
ATOM	2037	ND2	ASN	A	258	-1.732	20.324	66.946	1.00	149.86	A
ATOM	2038	C	ASN	A	258	-0.627	17.576	67.064	1.00	150.47	A
ATOM	2039	O	ASN	A	258	-1.557	17.989	67.758	1.00	150.47	A
ATOM	2040	N	TYR	A	259	-0.294	16.290	66.999	1.00	138.22	A
ATOM	2041	CA	TYR	A	259	-1.036	15.289	67.755	1.00	138.22	A
ATOM	2042	CB	TYR	A	259	-2.447	15.151	67.181	1.00	99.01	A
ATOM	2043	CG	TYR	A	259	-3.458	14.566	68.141	1.00	99.01	A
ATOM	2044	CD1	TYR	A	259	-3.942	15.311	69.216	1.00	99.01	A

FIGURE 25 CON'T

```
ATOM   2045  CE1 TYR A 259      -4.893  14.783  70.089  1.00 99.01      A
ATOM   2046  CD2 TYR A 259      -3.948  13.274  67.965  1.00 99.01      A
ATOM   2047  CE2 TYR A 259      -4.897  12.737  68.829  1.00 99.01      A
ATOM   2048  CZ  TYR A 259      -5.366  13.496  69.886  1.00 99.01      A
ATOM   2049  OH  TYR A 259      -6.314  12.968  70.732  1.00 99.01      A
ATOM   2050  C   TYR A 259      -0.344  13.928  67.734  1.00138.22      A
ATOM   2051  O   TYR A 259       0.060  13.410  68.776  1.00138.22      A
ATOM   2052  N   LYS A 260      -0.215  13.355  66.540  1.00 83.39      A
ATOM   2053  CA  LYS A 260       0.415  12.048  66.362  1.00 83.39      A
ATOM   2054  CB  LYS A 260       1.852  12.061  66.897  1.00 85.61      A
ATOM   2055  CG  LYS A 260       2.822  12.856  66.033  1.00 85.61      A
ATOM   2056  CD  LYS A 260       4.250  12.788  66.563  1.00 85.61      A
ATOM   2057  CE  LYS A 260       4.365  13.409  67.946  1.00 85.61      A
ATOM   2058  NZ  LYS A 260       3.853  14.806  67.967  1.00 85.61      A
ATOM   2059  C   LYS A 260      -0.374  10.914  67.016  1.00 83.39      A
ATOM   2060  O   LYS A 260      -0.565  10.884  68.231  1.00 83.39      A
ATOM   2061  N   ILE A 261      -0.829   9.985  66.184  1.00 62.77      A
ATOM   2062  CA  ILE A 261      -1.608   8.831  66.621  1.00 62.77      A
ATOM   2063  CB  ILE A 261      -3.003   8.802  65.923  1.00 58.19      A
ATOM   2064  CG2 ILE A 261      -3.803   7.598  66.380  1.00 58.19      A
ATOM   2065  CG1 ILE A 261      -3.774  10.091  66.227  1.00 58.19      A
ATOM   2066  CD1 ILE A 261      -3.252  11.311  65.498  1.00 58.19      A
ATOM   2067  C   ILE A 261      -0.863   7.550  66.251  1.00 62.77      A
ATOM   2068  O   ILE A 261      -0.047   7.541  65.328  1.00 62.77      A
ATOM   2069  N   TYR A 262      -1.141   6.475  66.981  1.00 45.49      A
ATOM   2070  CA  TYR A 262      -0.529   5.178  66.715  1.00 45.49      A
ATOM   2071  CB  TYR A 262      -0.166   4.465  68.019  1.00 68.83      A
ATOM   2072  CG  TYR A 262       1.284   4.622  68.423  1.00 68.83      A
ATOM   2073  CD1 TYR A 262       2.311   4.218  67.571  1.00 68.83      A
ATOM   2074  CE1 TYR A 262       3.647   4.353  67.939  1.00 68.83      A
ATOM   2075  CD2 TYR A 262       1.630   5.167  69.656  1.00 68.83      A

ATOM   2076  CE2 TYR A 262       2.959   5.306  70.035  1.00 68.83      A
ATOM   2077  CZ  TYR A 262       3.964   4.897  69.174  1.00 68.83      A
ATOM   2078  OH  TYR A 262       5.284   5.034  69.546  1.00 68.83      A
ATOM   2079  C   TYR A 262      -1.541   4.342  65.948  1.00 45.49      A
ATOM   2080  O   TYR A 262      -2.726   4.297  66.309  1.00 45.49      A
ATOM   2081  N   LEU A 263      -1.076   3.687  64.888  1.00 40.09      A
ATOM   2082  CA  LEU A 263      -1.948   2.853  64.070  1.00 40.09      A
ATOM   2083  CB  LEU A 263      -2.014   3.393  62.633  1.00 50.45      A
ATOM   2084  CG  LEU A 263      -2.482   4.837  62.440  1.00 50.45      A
ATOM   2085  CD1 LEU A 263      -2.321   5.233  60.970  1.00 50.45      A
ATOM   2086  CD2 LEU A 263      -3.929   4.974  62.901  1.00 50.45      A
ATOM   2087  C   LEU A 263      -1.441   1.423  64.025  1.00 40.09      A
ATOM   2088  O   LEU A 263      -0.236   1.172  64.097  1.00 40.09      A
ATOM   2089  N   LEU A 264      -2.369   0.486  63.903  1.00 45.51      A
ATOM   2090  CA  LEU A 264      -2.017  -0.921  63.809  1.00 45.51      A
ATOM   2091  CB  LEU A 264      -2.868  -1.752  64.772  1.00 44.81      A
ATOM   2092  CG  LEU A 264      -2.442  -1.822  66.245  1.00 44.81      A
ATOM   2093  CD1 LEU A 264      -2.185  -0.438  66.816  1.00 44.81      A
ATOM   2094  CD2 LEU A 264      -3.531  -2.534  67.030  1.00 44.81      A
ATOM   2095  C   LEU A 264      -2.271  -1.373  62.364  1.00 45.51      A
ATOM   2096  O   LEU A 264      -3.409  -1.350  61.896  1.00 45.51      A
ATOM   2097  N   PRO A 265      -1.206  -1.766  61.639  1.00 47.17      A
ATOM   2098  CD  PRO A 265       0.196  -1.780  62.082  1.00 53.05      A
ATOM   2099  CA  PRO A 265      -1.309  -2.223  60.249  1.00 47.17      A
ATOM   2100  CB  PRO A 265       0.105  -2.733  59.935  1.00 53.05      A
```

FIGURE 25 CON'T

```
ATOM   2101  CG  PRO A 265       0.752  -2.908  61.273  1.00 53.05      A
ATOM   2102  C   PRO A 265      -2.375  -3.289  60.054  1.00 47.17      A
ATOM   2103  O   PRO A 265      -2.897  -3.482  58.951  1.00 47.17      A
ATOM   2104  N   GLN A 266      -2.705  -3.954  61.154  1.00 44.41      A
ATOM   2105  CA  GLN A 266      -3.703  -5.014  61.188  1.00 44.41      A
ATOM   2106  CB  GLN A 266      -3.555  -5.805  62.500  1.00 52.67      A
ATOM   2107  CG  GLN A 266      -4.446  -7.029  62.628  1.00 52.67      A
ATOM   2108  CD  GLN A 266      -4.397  -7.640  64.026  1.00 52.67      A
ATOM   2109  OE1 GLN A 266      -3.465  -7.390  64.789  1.00 52.67      A
ATOM   2110  NE2 GLN A 266      -5.399  -8.453  64.361  1.00 52.67      A
ATOM   2111  C   GLN A 266      -5.109  -4.439  61.111  1.00 44.41      A
ATOM   2112  O   GLN A 266      -6.053  -5.141  60.757  1.00 44.41      A
ATOM   2113  N   LEU A 267      -5.243  -3.162  61.449  1.00 42.63      A
ATOM   2114  CA  LEU A 267      -6.548  -2.518  61.459  1.00 42.63      A
ATOM   2115  CB  LEU A 267      -6.815  -1.935  62.851  1.00 46.28      A
ATOM   2116  CG  LEU A 267      -6.670  -2.853  64.069  1.00 46.28      A
ATOM   2117  CD1 LEU A 267      -6.996  -2.057  65.324  1.00 46.28      A
ATOM   2118  CD2 LEU A 267      -7.597  -4.056  63.942  1.00 46.28      A
ATOM   2119  C   LEU A 267      -6.749  -1.411  60.430  1.00 42.63      A
ATOM   2120  O   LEU A 267      -7.811  -0.782  60.403  1.00 42.63      A
ATOM   2121  N   VAL A 268      -5.743  -1.154  59.599  1.00 50.36      A
ATOM   2122  CA  VAL A 268      -5.853  -0.092  58.605  1.00 50.36      A
ATOM   2123  CB  VAL A 268      -4.875   1.049  58.898  1.00 36.71      A
ATOM   2124  CG1 VAL A 268      -5.222   1.693  60.228  1.00 36.71      A
ATOM   2125  CG2 VAL A 268      -3.425   0.520  58.869  1.00 36.71      A
ATOM   2126  C   VAL A 268      -5.605  -0.532  57.171  1.00 50.36      A
ATOM   2127  O   VAL A 268      -4.858  -1.474  56.908  1.00 50.36      A
ATOM   2128  N   VAL A 269      -6.227   0.177  56.239  1.00 41.89      A
ATOM   2129  CA  VAL A 269      -6.054  -0.144  54.834  1.00 41.89      A
ATOM   2130  CB  VAL A 269      -7.389  -0.501  54.162  1.00 36.78      A
ATOM   2131  CG1 VAL A 269      -8.045  -1.675  54.879  1.00 36.78      A
ATOM   2132  CG2 VAL A 269      -8.293   0.711  54.150  1.00 36.78      A
ATOM   2133  C   VAL A 269      -5.463   1.028  54.071  1.00 41.89      A
ATOM   2134  O   VAL A 269      -5.777   2.186  54.345  1.00 41.89      A
ATOM   2135  N   PRO A 270      -4.566   0.738  53.125  1.00 45.86      A
ATOM   2136  CD  PRO A 270      -3.742  -0.476  53.021  1.00 42.86      A
ATOM   2137  CA  PRO A 270      -3.989   1.841  52.359  1.00 45.86      A
ATOM   2138  CB  PRO A 270      -2.840   1.180  51.579  1.00 42.86      A
ATOM   2139  CG  PRO A 270      -3.074  -0.279  51.704  1.00 42.86      A
ATOM   2140  C   PRO A 270      -5.063   2.467  51.458  1.00 45.86      A
ATOM   2141  O   PRO A 270      -5.921   1.766  50.914  1.00 45.86      A
ATOM   2142  N   THR A 271      -5.027   3.790  51.341  1.00 47.94      A
ATOM   2143  CA  THR A 271      -5.987   4.526  50.524  1.00 47.94      A
ATOM   2144  CB  THR A 271      -7.025   5.267  51.381  1.00 76.25      A
ATOM   2145  OG1 THR A 271      -7.294   4.516  52.570  1.00 76.25      A
ATOM   2146  CG2 THR A 271      -8.316   5.439  50.601  1.00 76.25      A
ATOM   2147  C   THR A 271      -5.224   5.570  49.731  1.00 47.94      A
ATOM   2148  O   THR A 271      -4.190   6.065  50.186  1.00 47.94      A
ATOM   2149  N   TYR A 272      -5.750   5.918  48.561  1.00 43.35      A
ATOM   2150  CA  TYR A 272      -5.112   6.890  47.676  1.00 43.35      A
ATOM   2151  CB  TYR A 272      -4.320   6.167  46.583  1.00 43.00      A
ATOM   2152  CG  TYR A 272      -3.239   5.233  47.053  1.00 43.00      A
ATOM   2153  CD1 TYR A 272      -1.992   5.722  47.442  1.00 43.00      A
ATOM   2154  CE1 TYR A 272      -0.987   4.868  47.855  1.00 43.00      A
ATOM   2155  CD2 TYR A 272      -3.454   3.855  47.091  1.00 43.00      A
ATOM   2156  CE2 TYR A 272      -2.453   2.984  47.502  1.00 43.00      A
ATOM   2157  CZ  TYR A 272      -1.222   3.498  47.883  1.00 43.00      A
```

FIGURE 25 CON'T

```
ATOM   2158  OH  TYR A 272      -0.222   2.652  48.291  1.00 43.00      A
ATOM   2159  C   TYR A 272      -6.130   7.769  46.956  1.00 43.35      A
ATOM   2160  O   TYR A 272      -7.227   7.311  46.620  1.00 43.35      A
ATOM   2161  N   ASN A 273      -5.764   9.029  46.728  1.00 37.52      A
ATOM   2162  CA  ASN A 273      -6.613   9.929  45.948  1.00 37.52      A
ATOM   2163  CB  ASN A 273      -6.359  11.398  46.300  1.00 68.70      A
ATOM   2164  CG  ASN A 273      -6.931  11.774  47.656  1.00 68.70      A
ATOM   2165  OD1 ASN A 273      -8.059  11.400  47.989  1.00 68.70      A
ATOM   2166  ND2 ASN A 273      -6.158  12.521  48.445  1.00 68.70      A
ATOM   2167  C   ASN A 273      -6.136   9.629  44.527  1.00 37.52      A
ATOM   2168  O   ASN A 273      -4.990   9.922  44.175  1.00 37.52      A
ATOM   2169  N   ALA A 274      -6.988   9.002  43.728  1.00 38.51      A
ATOM   2170  CA  ALA A 274      -6.609   8.629  42.359  1.00 38.51      A
ATOM   2171  CB  ALA A 274      -7.815   8.069  41.615  1.00 48.04      A
ATOM   2172  C   ALA A 274      -6.013   9.782  41.565  1.00 38.51      A
ATOM   2173  O   ALA A 274      -4.946   9.649  40.966  1.00 38.51      A
ATOM   2174  N   GLU A 275      -6.706  10.915  41.580  1.00 46.05      A
ATOM   2175  CA  GLU A 275      -6.279  12.098  40.846  1.00 46.05      A
ATOM   2176  CB  GLU A 275      -7.351  13.193  40.948  1.00 49.75      A
ATOM   2177  CG  GLU A 275      -8.585  13.001  40.029  1.00 49.75      A
ATOM   2178  CD  GLU A 275      -9.477  11.819  40.403  1.00 49.75      A
ATOM   2179  OE1 GLU A 275      -9.694  11.589  41.609  1.00 49.75      A
ATOM   2180  OE2 GLU A 275      -9.982  11.128  39.485  1.00 49.75      A
ATOM   2181  C   GLU A 275      -4.928  12.654  41.299  1.00 46.05      A
ATOM   2182  O   GLU A 275      -4.297  13.422  40.580  1.00 46.05      A
ATOM   2183  N   GLN A 276      -4.487  12.256  42.486  1.00 62.96      A
ATOM   2184  CA  GLN A 276      -3.215  12.717  43.036  1.00 62.96      A
ATOM   2185  CB  GLN A 276      -3.300  12.738  44.566  1.00 90.77      A
ATOM   2186  CG  GLN A 276      -2.027  13.162  45.274  1.00 90.77      A
ATOM   2187  CD  GLN A 276      -2.101  12.943  46.775  1.00 90.77      A
ATOM   2188  OE1 GLN A 276      -2.984  13.477  47.449  1.00 90.77      A
ATOM   2189  NE2 GLN A 276      -1.173  12.149  47.305  1.00 90.77      A
ATOM   2190  C   GLN A 276      -2.036  11.844  42.601  1.00 62.96      A
ATOM   2191  O   GLN A 276      -0.881  12.209  42.804  1.00 62.96      A
ATOM   2192  N   LEU A 277      -2.326  10.693  42.005  1.00 55.21      A
ATOM   2193  CA  LEU A 277      -1.271   9.786  41.568  1.00 55.21      A
ATOM   2194  CB  LEU A 277      -1.759   8.337  41.656  1.00 51.32      A
ATOM   2195  CG  LEU A 277      -2.321   7.937  43.025  1.00 51.32      A
ATOM   2196  CD1 LEU A 277      -2.811   6.487  42.999  1.00 51.32      A
ATOM   2197  CD2 LEU A 277      -1.247   8.132  44.082  1.00 51.32      A
ATOM   2198  C   LEU A 277      -0.823  10.093  40.140  1.00 55.21      A
ATOM   2199  O   LEU A 277      -1.622  10.554  39.317  1.00 55.21      A
ATOM   2200  N   ALA A 282      -2.259   2.294  38.184  1.00112.07      A
ATOM   2201  CA  ALA A 282      -1.574   1.210  37.496  1.00112.07      A
ATOM   2202  CB  ALA A 282      -2.064  -0.138  38.011  1.00 57.82      A
ATOM   2203  C   ALA A 282      -1.805   1.306  36.000  1.00112.07      A

ATOM   2204  O   ALA A 282      -1.167   2.102  35.316  1.00112.07      A
ATOM   2205  N   LYS A 283      -2.730   0.502  35.491  1.00 65.34      A
ATOM   2206  CA  LYS A 283      -3.013   0.506  34.061  1.00 65.34      A
ATOM   2207  CB  LYS A 283      -2.276  -0.663  33.389  1.00114.62      A
ATOM   2208  CG  LYS A 283      -0.953  -1.023  34.079  1.00114.62      A
ATOM   2209  CD  LYS A 283       0.197  -1.284  33.104  1.00114.62      A
ATOM   2210  CE  LYS A 283       0.076  -2.626  32.395  1.00114.62      A
ATOM   2211  NZ  LYS A 283      -1.071  -2.674  31.451  1.00114.62      A
ATOM   2212  C   LYS A 283      -4.515   0.376  33.860  1.00 65.34      A
ATOM   2213  O   LYS A 283      -5.162   1.247  33.273  1.00 65.34      A
```

FIGURE 25 CON'T

```
ATOM   2214  N   GLU A 284      -5.055  -0.729  34.360  1.00 67.78      A
ATOM   2215  CA  GLU A 284      -6.475  -1.019  34.291  1.00 67.78      A
ATOM   2216  CB  GLU A 284      -6.741  -2.436  34.795  1.00154.43      A
ATOM   2217  CG  GLU A 284      -6.135  -3.521  33.929  1.00154.43      A
ATOM   2218  CD  GLU A 284      -5.826  -4.777  34.713  1.00154.43      A
ATOM   2219  OE1 GLU A 284      -4.972  -4.706  35.622  1.00154.43      A
ATOM   2220  OE2 GLU A 284      -6.434  -5.830  34.425  1.00154.43      A
ATOM   2221  C   GLU A 284      -7.202  -0.020  35.172  1.00 67.78      A
ATOM   2222  O   GLU A 284      -8.275   0.468  34.812  1.00 67.78      A
ATOM   2223  N   ILE A 285      -6.621   0.281  36.333  1.00 59.11      A
ATOM   2224  CA  ILE A 285      -7.244   1.243  37.233  1.00 59.11      A
ATOM   2225  CB  ILE A 285      -6.463   1.414  38.555  1.00 56.69      A
ATOM   2226  CG2 ILE A 285      -6.974   2.657  39.305  1.00 56.69      A
ATOM   2227  CG1 ILE A 285      -6.629   0.165  39.420  1.00 56.69      A
ATOM   2228  CD1 ILE A 285      -5.905   0.227  40.746  1.00 56.69      A
ATOM   2229  C   ILE A 285      -7.296   2.588  36.538  1.00 59.11      A
ATOM   2230  O   ILE A 285      -8.374   3.134  36.295  1.00 59.11      A
ATOM   2231  N   LEU A 286      -6.117   3.108  36.212  1.00 87.11      A
ATOM   2232  CA  LEU A 286      -5.993   4.393  35.541  1.00 87.11      A
ATOM   2233  CB  LEU A 286      -4.648   4.482  34.821  1.00 84.12      A
ATOM   2234  CG  LEU A 286      -4.369   5.809  34.112  1.00 84.12      A
ATOM   2235  CD1 LEU A 286      -4.314   6.926  35.149  1.00 84.12      A
ATOM   2236  CD2 LEU A 286      -3.063   5.726  33.331  1.00 84.12      A
ATOM   2237  C   LEU A 286      -7.119   4.599  34.540  1.00 87.11      A
ATOM   2238  O   LEU A 286      -7.734   5.659  34.499  1.00 87.11      A
ATOM   2239  N   GLU A 287      -7.387   3.581  33.734  1.00 74.75      A
ATOM   2240  CA  GLU A 287      -8.442   3.664  32.739  1.00 74.75      A
ATOM   2241  CB  GLU A 287      -8.646   2.308  32.058  1.00118.41      A
ATOM   2242  CG  GLU A 287      -7.445   1.801  31.278  1.00118.41      A
ATOM   2243  CD  GLU A 287      -7.669   0.416  30.691  1.00118.41      A
ATOM   2244  OE1 GLU A 287      -6.762  -0.090  29.997  1.00118.41      A
ATOM   2245  OE2 GLU A 287      -8.750  -0.167  30.926  1.00118.41      A
ATOM   2246  C   GLU A 287      -9.748   4.089  33.393  1.00 74.75      A
ATOM   2247  O   GLU A 287     -10.250   5.183  33.143  1.00 74.75      A
ATOM   2248  N   TYR A 288     -10.277   3.218  34.247  1.00 53.07      A
ATOM   2249  CA  TYR A 288     -11.540   3.443  34.938  1.00 53.07      A
ATOM   2250  CB  TYR A 288     -11.732   2.396  36.047  1.00 53.22      A
ATOM   2251  CG  TYR A 288     -13.171   2.281  36.487  1.00 53.22      A
ATOM   2252  CD1 TYR A 288     -14.131   1.767  35.622  1.00 53.22      A
ATOM   2253  CE1 TYR A 288     -15.470   1.722  35.972  1.00 53.22      A
ATOM   2254  CD2 TYR A 288     -13.588   2.747  37.733  1.00 53.22      A
ATOM   2255  CE2 TYR A 288     -14.940   2.707  38.100  1.00 53.22      A
ATOM   2256  CZ  TYR A 288     -15.873   2.194  37.205  1.00 53.22      A
ATOM   2257  OH  TYR A 288     -17.218   2.171  37.516  1.00 53.22      A
ATOM   2258  C   TYR A 288     -11.736   4.834  35.533  1.00 53.07      A
ATOM   2259  O   TYR A 288     -12.866   5.315  35.628  1.00 53.07      A
ATOM   2260  N   THR A 289     -10.645   5.471  35.947  1.00 51.30      A
ATOM   2261  CA  THR A 289     -10.723   6.801  36.542  1.00 51.30      A
ATOM   2262  CB  THR A 289      -9.546   7.052  37.477  1.00 45.40      A
ATOM   2263  OG1 THR A 289      -8.329   6.831  36.759  1.00 45.40      A
ATOM   2264  CG2 THR A 289      -9.606   6.119  38.679  1.00 45.40      A
ATOM   2265  C   THR A 289     -10.732   7.901  35.489  1.00 51.30      A
ATOM   2266  O   THR A 289     -11.073   9.047  35.774  1.00 51.30      A
ATOM   2267  N   LYS A 290     -10.346   7.563  34.269  1.00 45.85      A
ATOM   2268  CA  LYS A 290     -10.338   8.555  33.211  1.00 45.85      A
ATOM   2269  CB  LYS A 290      -9.221   8.260  32.210  1.00 58.48      A
ATOM   2270  CG  LYS A 290      -7.825   8.280  32.843  1.00 58.48      A
```

FIGURE 25 CON'T

```
ATOM   2271  CD  LYS A 290      -7.517   9.621  33.528  1.00 58.48      A
ATOM   2272  CE  LYS A 290      -7.372  10.758  32.508  1.00 58.48      A
ATOM   2273  NZ  LYS A 290      -7.339  12.131  33.106  1.00 58.48      A
ATOM   2274  C   LYS A 290     -11.709   8.544  32.547  1.00 45.85      A
ATOM   2275  O   LYS A 290     -12.184   7.509  32.082  1.00 45.85      A
ATOM   2276  N   LEU A 291     -12.354   9.701  32.546  1.00 45.06      A
ATOM   2277  CA  LEU A 291     -13.677   9.843  31.973  1.00 45.06      A
ATOM   2278  CB  LEU A 291     -14.662  10.308  33.056  1.00 38.73      A
ATOM   2279  CG  LEU A 291     -14.897   9.348  34.231  1.00 38.73      A
ATOM   2280  CD1 LEU A 291     -15.715  10.018  35.319  1.00 38.73      A
ATOM   2281  CD2 LEU A 291     -15.621   8.082  33.715  1.00 38.73      A
ATOM   2282  C   LEU A 291     -13.659  10.847  30.831  1.00 45.06      A
ATOM   2283  O   LEU A 291     -13.199  11.979  30.988  1.00 45.06      A
ATOM   2284  N   MSE A 292     -14.160  10.427  29.679  1.00 39.88      A
ATOM   2285  CA  MSE A 292     -14.232  11.300  28.512  1.00 39.88      A
ATOM   2286  CB  MSE A 292     -14.791  10.531  27.310  1.00 87.18      A
ATOM   2287  CG  MSE A 292     -13.928   9.368  26.842  1.00 87.18      A
ATOM   2288  SE  MSE A 292     -12.260   9.931  26.037  1.00 87.18      A
ATOM   2289  CE  MSE A 292     -12.831   9.966  24.187  1.00 87.18      A
ATOM   2290  C   MSE A 292     -15.155  12.469  28.847  1.00 39.88      A
ATOM   2291  O   MSE A 292     -16.013  12.360  29.726  1.00 39.88      A
ATOM   2292  N   PRO A 293     -14.985  13.607  28.156  1.00 44.59      A
ATOM   2293  CD  PRO A 293     -13.958  13.862  27.127  1.00 38.08      A
ATOM   2294  CA  PRO A 293     -15.814  14.794  28.383  1.00 44.59      A
ATOM   2295  CB  PRO A 293     -15.418  15.716  27.232  1.00 38.08      A
ATOM   2296  CG  PRO A 293     -13.959  15.360  27.019  1.00 38.08      A
ATOM   2297  C   PRO A 293     -17.315  14.488  28.378  1.00 44.59      A
ATOM   2298  O   PRO A 293     -18.063  15.006  29.210  1.00 44.59      A
ATOM   2299  N   GLU A 294     -17.760  13.645  27.447  1.00 39.36      A
ATOM   2300  CA  GLU A 294     -19.186  13.319  27.361  1.00 39.36      A
ATOM   2301  CB  GLU A 294     -19.519  12.704  25.996  1.00 76.95      A
ATOM   2302  CG  GLU A 294     -19.579  13.729  24.856  1.00 76.95      A
ATOM   2303  CD  GLU A 294     -20.615  14.834  25.093  1.00 76.95      A
ATOM   2304  OE1 GLU A 294     -21.799  14.502  25.329  1.00 76.95      A
ATOM   2305  OE2 GLU A 294     -20.250  16.034  25.039  1.00 76.95      A
ATOM   2306  C   GLU A 294     -19.678  12.410  28.490  1.00 39.36      A
ATOM   2307  O   GLU A 294     -20.839  12.477  28.880  1.00 39.36      A
ATOM   2308  N   GLU A 295     -18.798  11.561  29.007  1.00 41.51      A
ATOM   2309  CA  GLU A 295     -19.165  10.679  30.110  1.00 41.51      A
ATOM   2310  CB  GLU A 295     -18.082   9.620  30.302  1.00 56.10      A
ATOM   2311  CG  GLU A 295     -17.764   8.902  29.009  1.00 56.10      A
ATOM   2312  CD  GLU A 295     -16.696   7.842  29.159  1.00 56.10      A
ATOM   2313  OE1 GLU A 295     -15.576   8.164  29.619  1.00 56.10      A
ATOM   2314  OE2 GLU A 295     -16.982   6.683  28.804  1.00 56.10      A
ATOM   2315  C   GLU A 295     -19.377  11.489  31.399  1.00 41.51      A
ATOM   2316  O   GLU A 295     -20.358  11.295  32.114  1.00 41.51      A
ATOM   2317  N   ARG A 296     -18.460  12.400  31.694  1.00 38.96      A
ATOM   2318  CA  ARG A 296     -18.592  13.237  32.885  1.00 38.96      A
ATOM   2319  CB  ARG A 296     -17.385  14.189  33.025  1.00 33.95      A
ATOM   2320  CG  ARG A 296     -16.105  13.523  33.582  1.00 33.95      A
ATOM   2321  CD  ARG A 296     -14.897  14.502  33.609  1.00 33.95      A
ATOM   2322  NE  ARG A 296     -13.694  13.815  34.068  1.00 33.95      A
ATOM   2323  CZ  ARG A 296     -13.390  13.605  35.352  1.00 33.95      A
ATOM   2324  NH1 ARG A 296     -14.200  14.050  36.307  1.00 33.95      A
ATOM   2325  NH2 ARG A 296     -12.296  12.908  35.680  1.00 33.95      A
ATOM   2326  C   ARG A 296     -19.871  14.049  32.755  1.00 38.96      A
ATOM   2327  O   ARG A 296     -20.634  14.170  33.707  1.00 38.96      A
```

FIGURE 25 CON'T

```
ATOM   2328  N   LYS A 297     -20.103  14.592  31.560  1.00 39.66      A
ATOM   2329  CA  LYS A 297     -21.286  15.408  31.300  1.00 39.66      A
ATOM   2330  CB  LYS A 297     -21.295  15.865  29.843  1.00 56.25      A
ATOM   2331  CG  LYS A 297     -22.431  16.814  29.479  1.00 56.25      A

ATOM   2332  CD  LYS A 297     -22.351  17.214  28.003  1.00 56.25      A
ATOM   2333  CE  LYS A 297     -23.438  18.198  27.634  1.00 56.25      A
ATOM   2334  NZ  LYS A 297     -24.802  17.627  27.845  1.00 56.25      A
ATOM   2335  C   LYS A 297     -22.563  14.629  31.607  1.00 39.66      A
ATOM   2336  O   LYS A 297     -23.444  15.103  32.340  1.00 39.66      A
ATOM   2337  N   GLU A 298     -22.651  13.430  31.042  1.00 40.20      A
ATOM   2338  CA  GLU A 298     -23.804  12.568  31.254  1.00 40.20      A
ATOM   2339  CB  GLU A 298     -23.665  11.314  30.397  1.00 70.61      A
ATOM   2340  CG  GLU A 298     -24.824  10.362  30.519  1.00 70.61      A
ATOM   2341  CD  GLU A 298     -24.775   9.264  29.482  1.00 70.61      A
ATOM   2342  OE1 GLU A 298     -25.751   8.494  29.398  1.00 70.61      A
ATOM   2343  OE2 GLU A 298     -23.764   9.168  28.750  1.00 70.61      A
ATOM   2344  C   GLU A 298     -23.965  12.169  32.727  1.00 40.20      A
ATOM   2345  O   GLU A 298     -25.065  12.244  33.274  1.00 40.20      A
ATOM   2346  N   LEU A 299     -22.878  11.731  33.366  1.00 39.60      A
ATOM   2347  CA  LEU A 299     -22.956  11.335  34.777  1.00 39.60      A
ATOM   2348  CB  LEU A 299     -21.585  10.868  35.284  1.00 34.67      A
ATOM   2349  CG  LEU A 299     -21.077   9.550  34.673  1.00 34.67      A
ATOM   2350  CD1 LEU A 299     -19.663   9.229  35.180  1.00 34.67      A
ATOM   2351  CD2 LEU A 299     -22.030   8.405  35.053  1.00 34.67      A
ATOM   2352  C   LEU A 299     -23.480  12.502  35.618  1.00 39.60      A
ATOM   2353  O   LEU A 299     -24.340  12.329  36.470  1.00 39.60      A
ATOM   2354  N   LEU A 300     -22.978  13.702  35.369  1.00 38.08      A
ATOM   2355  CA  LEU A 300     -23.459  14.858  36.117  1.00 38.08      A
ATOM   2356  CB  LEU A 300     -22.655  16.105  35.754  1.00 35.05      A
ATOM   2357  CG  LEU A 300     -21.217  16.121  36.295  1.00 35.05      A
ATOM   2358  CD1 LEU A 300     -20.608  17.488  35.994  1.00 35.05      A
ATOM   2359  CD2 LEU A 300     -21.214  15.844  37.820  1.00 35.05      A
ATOM   2360  C   LEU A 300     -24.950  15.106  35.852  1.00 38.08      A
ATOM   2361  O   LEU A 300     -25.715  15.422  36.775  1.00 38.08      A
ATOM   2362  N   GLU A 301     -25.364  14.979  34.595  1.00 40.84      A
ATOM   2363  CA  GLU A 301     -26.778  15.167  34.281  1.00 40.84      A
ATOM   2364  CB  GLU A 301     -27.013  15.099  32.764  1.00 49.55      A
ATOM   2365  CG  GLU A 301     -26.327  16.239  32.044  1.00 49.55      A
ATOM   2366  CD  GLU A 301     -26.457  16.181  30.544  1.00 49.55      A
ATOM   2367  OE1 GLU A 301     -26.651  15.075  29.996  1.00 49.55      A
ATOM   2368  OE2 GLU A 301     -26.344  17.251  29.912  1.00 49.55      A
ATOM   2369  C   GLU A 301     -27.615  14.108  35.002  1.00 40.84      A
ATOM   2370  O   GLU A 301     -28.724  14.391  35.418  1.00 40.84      A
ATOM   2371  N   ASN A 302     -27.075  12.900  35.164  1.00 46.53      A
ATOM   2372  CA  ASN A 302     -27.805  11.837  35.854  1.00 46.53      A
ATOM   2373  CB  ASN A 302     -27.052  10.513  35.784  1.00 44.80      A
ATOM   2374  CG  ASN A 302     -26.999   9.953  34.389  1.00 44.80      A
ATOM   2375  OD1 ASN A 302     -27.938  10.124  33.604  1.00 44.80      A
ATOM   2376  ND2 ASN A 302     -25.911   9.265  34.069  1.00 44.80      A
ATOM   2377  C   ASN A 302     -28.015  12.189  37.313  1.00 46.53      A
ATOM   2378  O   ASN A 302     -29.085  11.950  37.880  1.00 46.53      A
ATOM   2379  N   ILE A 303     -26.975  12.746  37.923  1.00 45.54      A
ATOM   2380  CA  ILE A 303     -27.036  13.141  39.319  1.00 45.54      A
ATOM   2381  CB  ILE A 303     -25.650  13.646  39.823  1.00 31.97      A
ATOM   2382  CG2 ILE A 303     -25.800  14.265  41.202  1.00 31.97      A
ATOM   2383  CG1 ILE A 303     -24.647  12.477  39.806  1.00 31.97      A
```

FIGURE 25 CON'T

```
ATOM   2384  CD1 ILE A 303     -23.167  12.888  39.983  1.00 31.97      A
ATOM   2385  C   ILE A 303     -28.056  14.250  39.467  1.00 45.54      A
ATOM   2386  O   ILE A 303     -28.868  14.246  40.398  1.00 45.54      A
ATOM   2387  N   LEU A 304     -28.014  15.198  38.539  1.00 47.06      A
ATOM   2388  CA  LEU A 304     -28.928  16.325  38.571  1.00 47.06      A
ATOM   2389  CB  LEU A 304     -28.582  17.325  37.467  1.00 43.97      A
ATOM   2390  CG  LEU A 304     -27.253  18.080  37.610  1.00 43.97      A
ATOM   2391  CD1 LEU A 304     -27.047  19.001  36.400  1.00 43.97      A
ATOM   2392  CD2 LEU A 304     -27.261  18.882  38.916  1.00 43.97      A
ATOM   2393  C   LEU A 304     -30.383  15.881  38.445  1.00 47.06      A
ATOM   2394  O   LEU A 304     -31.258  16.420  39.126  1.00 47.06      A
ATOM   2395  N   ALA A 305     -30.648  14.902  37.587  1.00 53.87      A
ATOM   2396  CA  ALA A 305     -32.016  14.419  37.420  1.00 53.87      A
ATOM   2397  CB  ALA A 305     -32.099  13.444  36.235  1.00 44.21      A
ATOM   2398  C   ALA A 305     -32.502  13.736  38.697  1.00 53.87      A
ATOM   2399  O   ALA A 305     -33.683  13.806  39.036  1.00 53.87      A
ATOM   2400  N   GLU A 306     -31.579  13.092  39.408  1.00 52.70      A
ATOM   2401  CA  GLU A 306     -31.895  12.382  40.643  1.00 52.70      A
ATOM   2402  CB  GLU A 306     -30.826  11.311  40.889  1.00 68.37      A
ATOM   2403  CG  GLU A 306     -31.346  10.015  41.479  1.00 68.37      A
ATOM   2404  CD  GLU A 306     -32.508   9.440  40.692  1.00 68.37      A
ATOM   2405  OE1 GLU A 306     -32.331   9.111  39.500  1.00 68.37      A
ATOM   2406  OE2 GLU A 306     -33.607   9.322  41.272  1.00 68.37      A
ATOM   2407  C   GLU A 306     -32.015  13.315  41.860  1.00 52.70      A
ATOM   2408  O   GLU A 306     -32.555  12.923  42.894  1.00 52.70      A
ATOM   2409  N   VAL A 307     -31.510  14.542  41.747  1.00 64.37      A
ATOM   2410  CA  VAL A 307     -31.605  15.497  42.851  1.00 64.37      A
ATOM   2411  CB  VAL A 307     -30.570  16.650  42.709  1.00 45.19      A
ATOM   2412  CG1 VAL A 307     -30.814  17.716  43.769  1.00 45.19      A
ATOM   2413  CG2 VAL A 307     -29.154  16.098  42.838  1.00 45.19      A
ATOM   2414  C   VAL A 307     -33.018  16.078  42.827  1.00 64.37      A
ATOM   2415  O   VAL A 307     -33.411  16.742  41.866  1.00 64.37      A
ATOM   2416  N   ASP A 308     -33.784  15.818  43.881  1.00 78.01      A
ATOM   2417  CA  ASP A 308     -35.158  16.300  43.950  1.00 78.01      A
ATOM   2418  CB  ASP A 308     -36.032  15.258  44.660  1.00109.90      A
ATOM   2419  CG  ASP A 308     -37.509  15.396  44.319  1.00109.90      A
ATOM   2420  OD1 ASP A 308     -37.862  15.270  43.125  1.00109.90      A
ATOM   2421  OD2 ASP A 308     -38.316  15.624  45.244  1.00109.90      A
ATOM   2422  C   ASP A 308     -35.250  17.646  44.670  1.00 78.01      A
ATOM   2423  O   ASP A 308     -35.921  17.768  45.693  1.00 78.01      A
ATOM   2424  N   SER A 309     -34.572  18.654  44.132  1.00 96.37      A
ATOM   2425  CA  SER A 309     -34.587  19.985  44.731  1.00 96.37      A
ATOM   2426  CB  SER A 309     -33.392  20.162  45.677  1.00 66.94      A
ATOM   2427  OG  SER A 309     -33.396  21.440  46.294  1.00 66.94      A
ATOM   2428  C   SER A 309     -34.546  21.048  43.647  1.00 96.37      A
ATOM   2429  O   SER A 309     -33.884  20.879  42.624  1.00 96.37      A
ATOM   2430  N   ASP A 310     -35.263  22.141  43.878  1.00 63.63      A
ATOM   2431  CA  ASP A 310     -35.311  23.239  42.926  1.00 63.63      A
ATOM   2432  CB  ASP A 310     -36.724  23.821  42.862  1.00124.85      A
ATOM   2433  CG  ASP A 310     -37.093  24.598  44.114  1.00124.85      A
ATOM   2434  OD1 ASP A 310     -37.104  24.003  45.214  1.00124.85      A
ATOM   2435  OD2 ASP A 310     -37.369  25.809  43.994  1.00124.85      A
ATOM   2436  C   ASP A 310     -34.330  24.336  43.329  1.00 63.63      A
ATOM   2437  O   ASP A 310     -34.211  25.351  42.639  1.00 63.63      A
ATOM   2438  N   ILE A 311     -33.626  24.134  44.442  1.00 57.09      A
ATOM   2439  CA  ILE A 311     -32.669  25.136  44.910  1.00 57.09      A
ATOM   2440  CB  ILE A 311     -32.072  24.752  46.283  1.00 68.75      A
```

FIGURE 25 CON'T

```
ATOM   2441  CG2 ILE A 311     -31.014  23.689  46.120  1.00 68.75      A
ATOM   2442  CG1 ILE A 311     -31.458  25.984  46.942  1.00 68.75      A
ATOM   2443  CD1 ILE A 311     -32.468  27.049  47.300  1.00 68.75      A
ATOM   2444  C   ILE A 311     -31.538  25.364  43.895  1.00 57.09      A
ATOM   2445  O   ILE A 311     -30.880  26.401  43.930  1.00 57.09      A
ATOM   2446  N   ILE A 312     -31.313  24.394  43.005  1.00 49.83      A
ATOM   2447  CA  ILE A 312     -30.297  24.520  41.952  1.00 49.83      A
ATOM   2448  CB  ILE A 312     -29.091  23.543  42.129  1.00 44.05      A
ATOM   2449  CG2 ILE A 312     -28.345  23.855  43.406  1.00 44.05      A
ATOM   2450  CG1 ILE A 312     -29.581  22.095  42.077  1.00 44.05      A
ATOM   2451  CD1 ILE A 312     -28.482  21.053  42.188  1.00 44.05      A
ATOM   2452  C   ILE A 312     -30.921  24.194  40.598  1.00 49.83      A
ATOM   2453  O   ILE A 312     -31.837  23.376  40.512  1.00 49.83      A
ATOM   2454  N   ASP A 313     -30.409  24.820  39.544  1.00 61.26      A
ATOM   2455  CA  ASP A 313     -30.907  24.568  38.199  1.00 61.26      A
ATOM   2456  CB  ASP A 313     -30.147  25.420  37.183  1.00 81.89      A
ATOM   2457  CG  ASP A 313     -30.753  26.806  37.017  1.00 81.89      A
ATOM   2458  OD1 ASP A 313     -31.077  27.455  38.040  1.00 81.89      A
ATOM   2459  OD2 ASP A 313     -30.900  27.248  35.858  1.00 81.89      A

ATOM   2460  C   ASP A 313     -30.780  23.092  37.861  1.00 61.26      A
ATOM   2461  O   ASP A 313     -30.002  22.367  38.481  1.00 61.26      A
ATOM   2462  N   LYS A 314     -31.550  22.651  36.874  1.00 58.31      A
ATOM   2463  CA  LYS A 314     -31.555  21.246  36.471  1.00 58.31      A
ATOM   2464  CB  LYS A 314     -32.964  20.854  36.022  1.00132.79      A
ATOM   2465  CG  LYS A 314     -33.545  21.781  34.965  1.00132.79      A
ATOM   2466  CD  LYS A 314     -34.952  21.369  34.574  1.00132.79      A
ATOM   2467  CE  LYS A 314     -35.524  22.302  33.519  1.00132.79      A
ATOM   2468  NZ  LYS A 314     -36.920  21.938  33.142  1.00132.79      A
ATOM   2469  C   LYS A 314     -30.554  20.907  35.372  1.00 58.31      A
ATOM   2470  O   LYS A 314     -30.297  19.739  35.098  1.00 58.31      A
ATOM   2471  N   SER A 315     -29.987  21.924  34.738  1.00 53.32      A
ATOM   2472  CA  SER A 315     -29.016  21.666  33.683  1.00 53.32      A
ATOM   2473  CB  SER A 315     -29.587  22.101  32.326  1.00 53.18      A
ATOM   2474  OG  SER A 315     -29.930  23.473  32.331  1.00 53.18      A
ATOM   2475  C   SER A 315     -27.678  22.355  33.941  1.00 53.32      A
ATOM   2476  O   SER A 315     -27.599  23.342  34.680  1.00 53.32      A
ATOM   2477  N   LEU A 316     -26.628  21.811  33.335  1.00 49.89      A
ATOM   2478  CA  LEU A 316     -25.277  22.350  33.467  1.00 49.89      A
ATOM   2479  CB  LEU A 316     -24.273  21.346  32.912  1.00 43.63      A
ATOM   2480  CG  LEU A 316     -24.223  19.999  33.633  1.00 43.63      A
ATOM   2481  CD1 LEU A 316     -23.395  19.019  32.811  1.00 43.63      A
ATOM   2482  CD2 LEU A 316     -23.638  20.186  35.041  1.00 43.63      A
ATOM   2483  C   LEU A 316     -25.129  23.677  32.723  1.00 49.89      A
ATOM   2484  O   LEU A 316     -25.695  23.859  31.646  1.00 49.89      A
ATOM   2485  N   SER A 317     -24.364  24.605  33.291  1.00 42.87      A
ATOM   2486  CA  SER A 317     -24.166  25.903  32.653  1.00 42.87      A
ATOM   2487  CB  SER A 317     -23.535  26.893  33.628  1.00 46.89      A
ATOM   2488  OG  SER A 317     -24.364  27.089  34.747  1.00 46.89      A
ATOM   2489  C   SER A 317     -23.252  25.777  31.443  1.00 42.87      A
ATOM   2490  O   SER A 317     -22.449  24.850  31.342  1.00 42.87      A
ATOM   2491  N   GLU A 318     -23.387  26.717  30.523  1.00 52.92      A
ATOM   2492  CA  GLU A 318     -22.546  26.746  29.338  1.00 52.92      A
ATOM   2493  CB  GLU A 318     -23.396  26.786  28.073  1.00 65.32      A
ATOM   2494  CG  GLU A 318     -24.597  25.883  28.122  1.00 65.32      A
ATOM   2495  CD  GLU A 318     -25.230  25.690  26.764  1.00 65.32      A
ATOM   2496  OE1 GLU A 318     -25.483  26.699  26.076  1.00 65.32      A
```

FIGURE 25 CON'T

```
ATOM   2497  OE2 GLU A 318     -25.478  24.523  26.393  1.00 65.32      A
ATOM   2498  C   GLU A 318     -21.778  28.048  29.475  1.00 52.92      A
ATOM   2499  O   GLU A 318     -22.210  28.945  30.196  1.00 52.92      A
ATOM   2500  N   ILE A 319     -20.643  28.168  28.802  1.00 42.77      A
ATOM   2501  CA  ILE A 319     -19.886  29.411  28.899  1.00 42.77      A
ATOM   2502  CB  ILE A 319     -18.871  29.362  30.072  1.00 47.55      A
ATOM   2503  CG2 ILE A 319     -17.739  28.389  29.745  1.00 47.55      A
ATOM   2504  CG1 ILE A 319     -18.295  30.759  30.326  1.00 47.55      A
ATOM   2505  CD1 ILE A 319     -17.438  30.865  31.581  1.00 47.55      A
ATOM   2506  C   ILE A 319     -19.153  29.694  27.596  1.00 42.77      A
ATOM   2507  O   ILE A 319     -18.750  28.781  26.886  1.00 42.77      A
ATOM   2508  N   GLU A 320     -18.998  30.967  27.269  1.00 53.70      A
ATOM   2509  CA  GLU A 320     -18.304  31.329  26.048  1.00 53.70      A
ATOM   2510  CB  GLU A 320     -18.747  32.716  25.581  1.00 79.12      A
ATOM   2511  CG  GLU A 320     -18.238  33.095  24.201  1.00 79.12      A
ATOM   2512  CD  GLU A 320     -18.813  34.414  23.717  1.00 79.12      A
ATOM   2513  OE1 GLU A 320     -18.512  35.462  24.329  1.00 79.12      A
ATOM   2514  OE2 GLU A 320     -19.575  34.399  22.726  1.00 79.12      A
ATOM   2515  C   GLU A 320     -16.816  31.329  26.350  1.00 53.70      A
ATOM   2516  O   GLU A 320     -16.374  31.945  27.318  1.00 53.70      A
ATOM   2517  N   VAL A 321     -16.055  30.621  25.527  1.00 54.10      A
ATOM   2518  CA  VAL A 321     -14.620  30.536  25.711  1.00 54.10      A
ATOM   2519  CB  VAL A 321     -14.174  29.067  26.004  1.00 40.96      A
ATOM   2520  CG1 VAL A 321     -15.018  28.481  27.118  1.00 40.96      A
ATOM   2521  CG2 VAL A 321     -14.275  28.220  24.760  1.00 40.96      A
ATOM   2522  C   VAL A 321     -13.892  31.038  24.465  1.00 54.10      A
ATOM   2523  O   VAL A 321     -14.487  31.175  23.388  1.00 54.10      A
ATOM   2524  N   GLU A 322     -12.605  31.322  24.628  1.00 50.68      A
ATOM   2525  CA  GLU A 322     -11.763  31.786  23.536  1.00 50.68      A
ATOM   2526  CB  GLU A 322     -10.832  32.906  24.012  1.00101.57      A
ATOM   2527  CG  GLU A 322     -11.453  34.292  24.060  1.00101.57      A
ATOM   2528  CD  GLU A 322     -11.649  34.886  22.677  1.00101.57      A
ATOM   2529  OE1 GLU A 322     -10.662  34.953  21.913  1.00101.57      A
ATOM   2530  OE2 GLU A 322     -12.786  35.290  22.354  1.00101.57      A
ATOM   2531  C   GLU A 322     -10.925  30.606  23.085  1.00 50.68      A
ATOM   2532  O   GLU A 322     -10.310  29.932  23.911  1.00 50.68      A
ATOM   2533  N   LYS A 323     -10.911  30.337  21.785  1.00 59.49      A
ATOM   2534  CA  LYS A 323     -10.105  29.241  21.270  1.00 59.49      A
ATOM   2535  CB  LYS A 323     -10.617  28.785  19.901  1.00 85.31      A
ATOM   2536  CG  LYS A 323     -11.995  28.148  19.941  1.00 85.31      A
ATOM   2537  CD  LYS A 323     -12.426  27.616  18.574  1.00 85.31      A
ATOM   2538  CE  LYS A 323     -12.598  28.740  17.553  1.00 85.31      A
ATOM   2539  NZ  LYS A 323     -13.134  28.250  16.247  1.00 85.31      A
ATOM   2540  C   LYS A 323      -8.687  29.786  21.154  1.00 59.49      A
ATOM   2541  O   LYS A 323      -8.479  30.993  21.271  1.00 59.49      A
ATOM   2542  N   ILE A 324      -7.713  28.906  20.951  1.00 55.83      A
ATOM   2543  CA  ILE A 324      -6.326  29.339  20.823  1.00 55.83      A
ATOM   2544  CB  ILE A 324      -5.417  28.644  21.873  1.00 54.86      A
ATOM   2545  CG2 ILE A 324      -3.964  29.066  21.675  1.00 54.86      A
ATOM   2546  CG1 ILE A 324      -5.882  29.014  23.285  1.00 54.86      A
ATOM   2547  CD1 ILE A 324      -5.103  28.336  24.374  1.00 54.86      A
ATOM   2548  C   ILE A 324      -5.849  29.005  19.413  1.00 55.83      A
ATOM   2549  O   ILE A 324      -5.957  27.860  18.972  1.00 55.83      A
ATOM   2550  N   ALA A 325      -5.328  30.014  18.719  1.00 63.86      A
ATOM   2551  CA  ALA A 325      -4.853  29.873  17.340  1.00 63.86      A
ATOM   2552  CB  ALA A 325      -4.255  31.201  16.867  1.00 53.96      A
ATOM   2553  C   ALA A 325      -3.855  28.745  17.113  1.00 63.86      A
```

FIGURE 25 CON'T

```
ATOM   2554  O   ALA A 325      -2.978  28.499  17.942  1.00 63.86      A
ATOM   2555  N   GLN A 326      -3.992  28.061  15.981  1.00 68.30      A
ATOM   2556  CA  GLN A 326      -3.095  26.963  15.639  1.00 68.30      A
ATOM   2557  CB  GLN A 326      -3.548  26.275  14.350  1.00137.18      A
ATOM   2558  CG  GLN A 326      -4.919  25.633  14.421  1.00137.18      A
ATOM   2559  CD  GLN A 326      -5.318  24.982  13.109  1.00137.18      A
ATOM   2560  OE1 GLN A 326      -5.411  25.645  12.076  1.00137.18      A
ATOM   2561  NE2 GLN A 326      -5.555  23.675  13.146  1.00137.18      A
ATOM   2562  C   GLN A 326      -1.691  27.513  15.444  1.00 68.30      A
ATOM   2563  O   GLN A 326      -0.710  26.777  15.522  1.00 68.30      A
ATOM   2564  N   GLU A 327      -1.608  28.817  15.193  1.00 63.72      A
ATOM   2565  CA  GLU A 327      -0.332  29.486  14.977  1.00 63.72      A
ATOM   2566  CB  GLU A 327      -0.561  30.941  14.564  1.00133.49      A
ATOM   2567  CG  GLU A 327       0.723  31.714  14.303  1.00133.49      A
ATOM   2568  CD  GLU A 327       0.503  33.215  14.263  1.00133.49      A
ATOM   2569  OE1 GLU A 327       1.459  33.950  13.933  1.00133.49      A
ATOM   2570  OE2 GLU A 327      -0.624  33.660  14.570  1.00133.49      A
ATOM   2571  C   GLU A 327       0.547  29.461  16.223  1.00 63.72      A
ATOM   2572  O   GLU A 327       1.763  29.316  16.126  1.00 63.72      A
ATOM   2573  N   LEU A 328      -0.074  29.623  17.389  1.00 61.48      A
ATOM   2574  CA  LEU A 328       0.660  29.628  18.653  1.00 61.48      A
ATOM   2575  CB  LEU A 328      -0.253  30.110  19.783  1.00 64.24      A
ATOM   2576  CG  LEU A 328      -0.757  31.547  19.614  1.00 64.24      A
ATOM   2577  CD1 LEU A 328      -1.830  31.866  20.646  1.00 64.24      A
ATOM   2578  CD2 LEU A 328       0.414  32.506  19.744  1.00 64.24      A
ATOM   2579  C   LEU A 328       1.218  28.241  18.972  1.00 61.48      A
ATOM   2580  O   LEU A 328       1.834  28.032  20.010  1.00 61.48      A
ATOM   2581  N   GLU A 329       1.001  27.307  18.053  1.00 61.19      A
ATOM   2582  CA  GLU A 329       1.464  25.935  18.187  1.00 61.19      A
ATOM   2583  CB  GLU A 329       0.471  24.975  17.529  1.00 79.60      A
ATOM   2584  CG  GLU A 329      -0.875  24.863  18.200  1.00 79.60      A
ATOM   2585  CD  GLU A 329      -0.838  23.942  19.394  1.00 79.60      A
ATOM   2586  OE1 GLU A 329      -0.423  22.776  19.229  1.00 79.60      A
ATOM   2587  OE2 GLU A 329      -1.224  24.382  20.494  1.00 79.60      A

ATOM   2588  C   GLU A 329       2.793  25.773  17.470  1.00 61.19      A
ATOM   2589  O   GLU A 329       3.492  24.778  17.667  1.00 61.19      A
ATOM   2590  N   ASN A 330       3.143  26.749  16.638  1.00 55.96      A
ATOM   2591  CA  ASN A 330       4.369  26.640  15.858  1.00 55.96      A
ATOM   2592  CB  ASN A 330       4.044  26.811  14.366  1.00 70.78      A
ATOM   2593  CG  ASN A 330       2.756  26.108  13.956  1.00 70.78      A
ATOM   2594  OD1 ASN A 330       2.566  24.921  14.218  1.00 70.78      A
ATOM   2595  ND2 ASN A 330       1.864  26.848  13.304  1.00 70.78      A
ATOM   2596  C   ASN A 330       5.488  27.605  16.232  1.00 55.96      A
ATOM   2597  O   ASN A 330       6.381  27.849  15.425  1.00 55.96      A
ATOM   2598  N   LYS A 331       5.462  28.143  17.443  1.00 43.12      A
ATOM   2599  CA  LYS A 331       6.495  29.095  17.831  1.00 43.12      A
ATOM   2600  CB  LYS A 331       5.958  30.016  18.924  1.00 70.20      A
ATOM   2601  CG  LYS A 331       4.812  30.887  18.417  1.00 70.20      A
ATOM   2602  CD  LYS A 331       4.619  32.131  19.261  1.00 70.20      A
ATOM   2603  CE  LYS A 331       3.665  33.108  18.578  1.00 70.20      A
ATOM   2604  NZ  LYS A 331       4.143  33.510  17.219  1.00 70.20      A
ATOM   2605  C   LYS A 331       7.840  28.490  18.237  1.00 43.12      A
ATOM   2606  O   LYS A 331       8.846  29.201  18.325  1.00 43.12      A
ATOM   2607  N   ILE A 332       7.870  27.176  18.449  1.00 45.53      A
ATOM   2608  CA  ILE A 332       9.100  26.502  18.836  1.00 45.53      A
ATOM   2609  CB  ILE A 332       8.854  25.576  20.054  1.00 52.84      A
```

FIGURE 25 CON'T

ATOM	2610	CG2	ILE	A	332	10.114	24.772	20.382	1.00	52.84	A
ATOM	2611	CG1	ILE	A	332	8.417	26.419	21.254	1.00	52.84	A
ATOM	2612	CD1	ILE	A	332	7.900	25.599	22.417	1.00	52.84	A
ATOM	2613	C	ILE	A	332	9.609	25.676	17.666	1.00	45.53	A
ATOM	2614	O	ILE	A	332	8.909	24.787	17.184	1.00	45.53	A
ATOM	2615	N	ARG	A	333	10.829	25.956	17.214	1.00	45.17	A
ATOM	2616	CA	ARG	A	333	11.383	25.215	16.082	1.00	45.17	A
ATOM	2617	CB	ARG	A	333	11.418	26.112	14.837	1.00	93.38	A
ATOM	2618	CG	ARG	A	333	10.064	26.641	14.388	1.00	93.38	A
ATOM	2619	CD	ARG	A	333	10.141	27.407	13.060	1.00	93.38	A
ATOM	2620	NE	ARG	A	333	10.929	28.637	13.145	1.00	93.38	A
ATOM	2621	CZ	ARG	A	333	12.258	28.691	13.082	1.00	93.38	A
ATOM	2622	NH1	ARG	A	333	12.967	27.581	12.928	1.00	93.38	A
ATOM	2623	NH2	ARG	A	333	12.882	29.859	13.178	1.00	93.38	A
ATOM	2624	C	ARG	A	333	12.781	24.624	16.291	1.00	45.17	A
ATOM	2625	O	ARG	A	333	13.519	25.027	17.202	1.00	45.17	A
ATOM	2626	N	VAL	A	334	13.123	23.664	15.429	1.00	59.14	A
ATOM	2627	CA	VAL	A	334	14.430	23.013	15.430	1.00	59.14	A
ATOM	2628	CB	VAL	A	334	14.369	21.557	15.970	1.00	47.97	A
ATOM	2629	CG1	VAL	A	334	14.003	21.570	17.456	1.00	47.97	A
ATOM	2630	CG2	VAL	A	334	13.363	20.736	15.173	1.00	47.97	A
ATOM	2631	C	VAL	A	334	14.925	23.001	13.986	1.00	59.14	A
ATOM	2632	O	VAL	A	334	14.134	23.150	13.051	1.00	59.14	A
ATOM	2633	N	ARG	A	335	16.225	22.816	13.794	1.00	54.77	A
ATOM	2634	CA	ARG	A	335	16.785	22.827	12.451	1.00	54.77	A
ATOM	2635	CB	ARG	A	335	17.499	24.162	12.214	1.00	63.65	A
ATOM	2636	CG	ARG	A	335	18.598	24.412	13.240	1.00	63.65	A
ATOM	2637	CD	ARG	A	335	19.398	25.676	12.990	1.00	63.65	A
ATOM	2638	NE	ARG	A	335	20.376	25.881	14.056	1.00	63.65	A
ATOM	2639	CZ	ARG	A	335	21.342	26.795	14.035	1.00	63.65	A
ATOM	2640	NH1	ARG	A	335	21.475	27.605	12.997	1.00	63.65	A
ATOM	2641	NH2	ARG	A	335	22.185	26.893	15.053	1.00	63.65	A
ATOM	2642	C	ARG	A	335	17.777	21.690	12.237	1.00	54.77	A
ATOM	2643	O	ARG	A	335	18.200	21.041	13.196	1.00	54.77	A
ATOM	2644	N	ASP	A	336	18.145	21.464	10.973	1.00	57.09	A
ATOM	2645	CA	ASP	A	336	19.117	20.430	10.615	1.00	57.09	A
ATOM	2646	CB	ASP	A	336	18.614	19.589	9.438	1.00	89.22	A
ATOM	2647	CG	ASP	A	336	18.159	20.434	8.268	1.00	89.22	A
ATOM	2648	OD1	ASP	A	336	18.929	21.312	7.826	1.00	89.22	A
ATOM	2649	OD2	ASP	A	336	17.029	20.211	7.787	1.00	89.22	A
ATOM	2650	C	ASP	A	336	20.451	21.098	10.258	1.00	57.09	A
ATOM	2651	O	ASP	A	336	20.592	22.317	10.399	1.00	57.09	A
ATOM	2652	N	ASP	A	337	21.425	20.309	9.807	1.00	74.53	A
ATOM	2653	CA	ASP	A	337	22.740	20.852	9.461	1.00	74.53	A
ATOM	2654	CB	ASP	A	337	23.794	19.739	9.446	1.00	86.24	A
ATOM	2655	CG	ASP	A	337	23.462	18.634	8.468	1.00	86.24	A
ATOM	2656	OD1	ASP	A	337	22.338	18.093	8.540	1.00	86.24	A
ATOM	2657	OD2	ASP	A	337	24.327	18.301	7.629	1.00	86.24	A
ATOM	2658	C	ASP	A	337	22.741	21.590	8.127	1.00	74.53	A
ATOM	2659	O	ASP	A	337	23.748	22.183	7.739	1.00	74.53	A
ATOM	2660	N	LYS	A	338	21.613	21.542	7.426	1.00	94.53	A
ATOM	2661	CA	LYS	A	338	21.476	22.235	6.152	1.00	94.53	A
ATOM	2662	CB	LYS	A	338	20.460	21.527	5.249	1.00	92.71	A
ATOM	2663	CG	LYS	A	338	20.999	20.319	4.490	1.00	92.71	A
ATOM	2664	CD	LYS	A	338	21.334	19.151	5.402	1.00	92.71	A
ATOM	2665	CE	LYS	A	338	21.821	17.954	4.592	1.00	92.71	A
ATOM	2666	NZ	LYS	A	338	22.167	16.779	5.444	1.00	92.71	A

FIGURE 25 CON'T

```
ATOM   2667  C   LYS A 338      20.997  23.648   6.452  1.00 94.53      A
ATOM   2668  O   LYS A 338      21.757  24.481   6.944  1.00 94.53      A
ATOM   2669  N   GLY A 339      19.728  23.908   6.165  1.00 93.63      A
ATOM   2670  CA  GLY A 339      19.164  25.219   6.423  1.00 93.63      A
ATOM   2671  C   GLY A 339      17.670  25.120   6.645  1.00 93.63      A
ATOM   2672  O   GLY A 339      16.958  26.123   6.594  1.00 93.63      A
ATOM   2673  N   ASN A 340      17.196  23.904   6.902  1.00 66.46      A
ATOM   2674  CA  ASN A 340      15.773  23.665   7.122  1.00 66.46      A
ATOM   2675  CB  ASN A 340      15.409  22.247   6.684  1.00 93.09      A
ATOM   2676  CG  ASN A 340      15.896  21.929   5.290  1.00 93.09      A
ATOM   2677  OD1 ASN A 340      17.097  21.962   5.019  1.00 93.09      A
ATOM   2678  ND2 ASN A 340      14.968  21.618   4.393  1.00 93.09      A
ATOM   2679  C   ASN A 340      15.326  23.878   8.570  1.00 66.46      A
ATOM   2680  O   ASN A 340      15.940  23.366   9.510  1.00 66.46      A
ATOM   2681  N   SER A 341      14.245  24.635   8.729  1.00 90.87      A
ATOM   2682  CA  SER A 341      13.675  24.928  10.036  1.00 90.87      A
ATOM   2683  CB  SER A 341      13.751  26.424  10.334  1.00 97.06      A
ATOM   2684  OG  SER A 341      15.093  26.865  10.405  1.00 97.06      A
ATOM   2685  C   SER A 341      12.218  24.493  10.047  1.00 90.87      A
ATOM   2686  O   SER A 341      11.420  24.942   9.226  1.00 90.87      A
ATOM   2687  N   VAL A 342      11.878  23.613  10.978  1.00 73.22      A
ATOM   2688  CA  VAL A 342      10.516  23.120  11.106  1.00 73.22      A
ATOM   2689  CB  VAL A 342      10.406  21.658  10.608  1.00 84.47      A
ATOM   2690  CG1 VAL A 342       9.030  21.096  10.927  1.00 84.47      A
ATOM   2691  CG2 VAL A 342      10.665  21.602   9.107  1.00 84.47      A
ATOM   2692  C   VAL A 342      10.096  23.185  12.570  1.00 73.22      A
ATOM   2693  O   VAL A 342      10.889  22.889  13.461  1.00 73.22      A
ATOM   2694  N   PRO A 343       8.847  23.599  12.837  1.00 65.78      A
ATOM   2695  CD  PRO A 343       7.871  24.164  11.886  1.00 66.06      A
ATOM   2696  CA  PRO A 343       8.350  23.689  14.215  1.00 65.78      A
ATOM   2697  CB  PRO A 343       7.115  24.574  14.075  1.00 66.06      A
ATOM   2698  CG  PRO A 343       6.605  24.214  12.708  1.00 66.06      A
ATOM   2699  C   PRO A 343       8.017  22.302  14.771  1.00 65.78      A
ATOM   2700  O   PRO A 343       7.633  21.401  14.019  1.00 65.78      A
ATOM   2701  N   ILE A 344       8.176  22.130  16.083  1.00 66.21      A
ATOM   2702  CA  ILE A 344       7.889  20.849  16.718  1.00 66.21      A
ATOM   2703  CB  ILE A 344       8.027  20.936  18.268  1.00 95.56      A
ATOM   2704  CG2 ILE A 344       7.364  19.732  18.928  1.00 95.56      A
ATOM   2705  CG1 ILE A 344       9.503  20.977  18.670  1.00 95.56      A
ATOM   2706  CD1 ILE A 344      10.266  22.154  18.127  1.00 95.56      A
ATOM   2707  C   ILE A 344       6.473  20.411  16.361  1.00 66.21      A
ATOM   2708  O   ILE A 344       5.504  20.847  16.984  1.00 66.21      A
ATOM   2709  N   SER A 345       6.367  19.555  15.347  1.00132.27      A
ATOM   2710  CA  SER A 345       5.085  19.033  14.877  1.00132.27      A
ATOM   2711  CB  SER A 345       4.191  20.171  14.377  1.00 71.12      A
ATOM   2712  OG  SER A 345       3.918  21.114  15.400  1.00 71.12      A
ATOM   2713  C   SER A 345       5.304  18.036  13.739  1.00132.27      A
ATOM   2714  O   SER A 345       5.223  18.400  12.566  1.00132.27      A
ATOM   2715  N   GLN A 346       5.587  16.783  14.087  1.00139.05      A

ATOM   2716  CA  GLN A 346       5.811  15.745  13.085  1.00139.05      A
ATOM   2717  CB  GLN A 346       7.228  15.171  13.204  1.00115.07      A
ATOM   2718  CG  GLN A 346       8.344  16.209  13.198  1.00115.07      A
ATOM   2719  CD  GLN A 346       8.739  16.660  14.595  1.00115.07      A
ATOM   2720  OE1 GLN A 346       7.906  17.122  15.372  1.00115.07      A
ATOM   2721  NE2 GLN A 346      10.020  16.527  14.918  1.00115.07      A
ATOM   2722  C   GLN A 346       4.794  14.616  13.241  1.00139.05      A
```

FIGURE 25 CON'T

```
ATOM   2723  O   GLN A 346       5.005  13.504  12.757  1.00139.05      A
ATOM   2724  N   LEU A 355       9.591   8.875  -2.331  1.00 72.02      A
ATOM   2725  CA  LEU A 355      10.136   9.754  -1.302  1.00 72.02      A
ATOM   2726  CB  LEU A 355       9.665   9.304   0.089  1.00 78.63      A
ATOM   2727  CG  LEU A 355       8.508  10.101   0.702  1.00 78.63      A
ATOM   2728  CD1 LEU A 355       7.944   9.358   1.900  1.00 78.63      A
ATOM   2729  CD2 LEU A 355       9.000  11.491   1.112  1.00 78.63      A
ATOM   2730  C   LEU A 355      11.663   9.823  -1.343  1.00 72.02      A
ATOM   2731  O   LEU A 355      12.309   9.182  -2.179  1.00 72.02      A
ATOM   2732  N   LEU A 356      12.225  10.611  -0.430  1.00 65.93      A
ATOM   2733  CA  LEU A 356      13.667  10.810  -0.330  1.00 65.93      A
ATOM   2734  CB  LEU A 356      13.992  11.618   0.931  1.00 79.78      A
ATOM   2735  CG  LEU A 356      15.435  12.095   1.087  1.00 79.78      A
ATOM   2736  CD1 LEU A 356      15.775  13.058  -0.039  1.00 79.78      A
ATOM   2737  CD2 LEU A 356      15.609  12.772   2.437  1.00 79.78      A
ATOM   2738  C   LEU A 356      14.447   9.496  -0.318  1.00 65.93      A
ATOM   2739  O   LEU A 356      14.209   8.617   0.514  1.00 65.93      A
ATOM   2740  N   TRP A 357      15.394   9.387  -1.245  1.00 61.77      A
ATOM   2741  CA  TRP A 357      16.223   8.199  -1.391  1.00 61.77      A
ATOM   2742  CB  TRP A 357      17.331   8.470  -2.422  1.00 64.38      A
ATOM   2743  CG  TRP A 357      18.220   9.633  -2.077  1.00 64.38      A
ATOM   2744  CD2 TRP A 357      19.646   9.611  -1.936  1.00 64.38      A
ATOM   2745  CE2 TRP A 357      20.055  10.924  -1.611  1.00 64.38      A
ATOM   2746  CE3 TRP A 357      20.619   8.610  -2.053  1.00 64.38      A
ATOM   2747  CD1 TRP A 357      17.833  10.926  -1.838  1.00 64.38      A
ATOM   2748  NE1 TRP A 357      18.930  11.705  -1.558  1.00 64.38      A
ATOM   2749  CZ2 TRP A 357      21.396  11.262  -1.401  1.00 64.38      A
ATOM   2750  CZ3 TRP A 357      21.952   8.946  -1.845  1.00 64.38      A
ATOM   2751  CH2 TRP A 357      22.327  10.264  -1.522  1.00 64.38      A
ATOM   2752  C   TRP A 357      16.842   7.679  -0.089  1.00 61.77      A
ATOM   2753  O   TRP A 357      16.840   6.468   0.161  1.00 61.77      A
ATOM   2754  N   THR A 358      17.356   8.590   0.738  1.00 70.70      A
ATOM   2755  CA  THR A 358      18.007   8.224   2.000  1.00 70.70      A
ATOM   2756  CB  THR A 358      18.856   9.400   2.550  1.00 65.54      A
ATOM   2757  OG1 THR A 358      18.031  10.564   2.680  1.00 65.54      A
ATOM   2758  CG2 THR A 358      20.027   9.705   1.617  1.00 65.54      A
ATOM   2759  C   THR A 358      17.094   7.746   3.132  1.00 70.70      A
ATOM   2760  O   THR A 358      17.583   7.380   4.204  1.00 70.70      A
ATOM   2761  N   ASN A 359      15.782   7.737   2.901  1.00 67.73      A
ATOM   2762  CA  ASN A 359      14.826   7.311   3.929  1.00 67.73      A
ATOM   2763  CB  ASN A 359      13.395   7.636   3.497  1.00 74.30      A
ATOM   2764  CG  ASN A 359      13.145   9.127   3.384  1.00 74.30      A
ATOM   2765  OD1 ASN A 359      13.878   9.935   3.956  1.00 74.30      A
ATOM   2766  ND2 ASN A 359      12.107   9.498   2.643  1.00 78.38      A
ATOM   2767  C   ASN A 359      14.862   5.820   4.260  1.00 67.73      A
ATOM   2768  O   ASN A 359      14.010   5.323   4.993  1.00 67.73      A
ATOM   2769  N   TYR A 360      15.847   5.105   3.730  1.00 69.19      A
ATOM   2770  CA  TYR A 360      15.956   3.673   3.988  1.00 69.19      A
ATOM   2771  CB  TYR A 360      16.561   2.970   2.774  1.00 54.50      A
ATOM   2772  CG  TYR A 360      18.044   3.230   2.629  1.00 54.50      A
ATOM   2773  CD1 TYR A 360      18.984   2.349   3.168  1.00 54.50      A
ATOM   2774  CE1 TYR A 360      20.352   2.617   3.085  1.00 54.50      A
ATOM   2775  CD2 TYR A 360      18.508   4.385   2.003  1.00 54.50      A
ATOM   2776  CE2 TYR A 360      19.871   4.662   1.917  1.00 54.50      A
ATOM   2777  CZ  TYR A 360      20.785   3.774   2.458  1.00 54.50      A
ATOM   2778  OH  TYR A 360      22.129   4.041   2.356  1.00 54.50      A
ATOM   2779  C   TYR A 360      16.832   3.379   5.203  1.00 69.19      A
```

FIGURE 25 CON'T

ATOM	2780	O	TYR	A	360	16.650	2.362	5.868	1.00 69.19	A
ATOM	2781	N	SER	A	361	17.782	4.268	5.486	1.00 60.27	A
ATOM	2782	CA	SER	A	361	18.713	4.061	6.597	1.00 60.27	A
ATOM	2783	CB	SER	A	361	19.987	4.898	6.387	1.00 72.15	A
ATOM	2784	OG	SER	A	361	19.745	6.275	6.608	1.00 72.15	A
ATOM	2785	C	SER	A	361	18.165	4.328	8.001	1.00 60.27	A
ATOM	2786	O	SER	A	361	17.225	5.104	8.191	1.00 60.27	A
ATOM	2787	N	ARG	A	362	18.786	3.671	8.979	1.00 65.79	A
ATOM	2788	CA	ARG	A	362	18.413	3.798	10.386	1.00 65.79	A
ATOM	2789	CB	ARG	A	362	18.830	2.537	11.153	1.00 83.77	A
ATOM	2790	CG	ARG	A	362	17.866	1.358	11.048	1.00 83.77	A
ATOM	2791	CD	ARG	A	362	17.631	0.927	9.612	1.00 83.77	A
ATOM	2792	NE	ARG	A	362	16.788	-0.264	9.522	1.00 83.77	A
ATOM	2793	CZ	ARG	A	362	17.185	-1.497	9.825	1.00 83.77	A
ATOM	2794	NH1	ARG	A	362	18.423	-1.718	10.244	1.00 83.77	A
ATOM	2795	NH2	ARG	A	362	16.343	-2.514	9.699	1.00 83.77	A
ATOM	2796	C	ARG	A	362	19.060	5.022	11.034	1.00 65.79	A
ATOM	2797	O	ARG	A	362	19.064	5.154	12.255	1.00 65.79	A
ATOM	2798	N	LYS	A	363	19.610	5.914	10.216	1.00 54.37	A
ATOM	2799	CA	LYS	A	363	20.257	7.123	10.723	1.00 54.37	A
ATOM	2800	CB	LYS	A	363	20.897	7.902	9.568	1.00103.89	A
ATOM	2801	CG	LYS	A	363	21.841	7.073	8.710	1.00103.89	A
ATOM	2802	CD	LYS	A	363	22.262	7.820	7.448	1.00103.89	A
ATOM	2803	CE	LYS	A	363	23.043	6.914	6.492	1.00103.89	A
ATOM	2804	NZ	LYS	A	363	23.344	7.575	5.185	1.00103.89	A
ATOM	2805	C	LYS	A	363	19.225	8.004	11.421	1.00 54.37	A
ATOM	2806	O	LYS	A	363	18.150	8.256	10.877	1.00 54.37	A
ATOM	2807	N	TYR	A	364	19.543	8.464	12.627	1.00 54.01	A
ATOM	2808	CA	TYR	A	364	18.627	9.331	13.363	1.00 54.01	A
ATOM	2809	CB	TYR	A	364	19.116	9.539	14.802	1.00 44.05	A
ATOM	2810	CG	TYR	A	364	18.352	8.759	15.845	1.00 44.05	A
ATOM	2811	CD1	TYR	A	364	17.691	9.416	16.888	1.00 44.05	A
ATOM	2812	CE1	TYR	A	364	16.968	8.710	17.838	1.00 44.05	A
ATOM	2813	CD2	TYR	A	364	18.272	7.373	15.784	1.00 44.05	A
ATOM	2814	CE2	TYR	A	364	17.551	6.659	16.732	1.00 44.05	A
ATOM	2815	CZ	TYR	A	364	16.899	7.334	17.755	1.00 44.05	A
ATOM	2816	OH	TYR	A	364	16.160	6.623	18.677	1.00 44.05	A
ATOM	2817	C	TYR	A	364	18.572	10.683	12.669	1.00 54.01	A
ATOM	2818	O	TYR	A	364	19.467	11.025	11.899	1.00 54.01	A
ATOM	2819	N	PRO	A	365	17.509	11.466	12.915	1.00 54.14	A
ATOM	2820	CD	PRO	A	365	16.304	11.223	13.730	1.00 56.06	A
ATOM	2821	CA	PRO	A	365	17.451	12.775	12.262	1.00 54.14	A
ATOM	2822	CB	PRO	A	365	16.075	13.309	12.666	1.00 56.06	A
ATOM	2823	CG	PRO	A	365	15.815	12.628	14.004	1.00 56.06	A
ATOM	2824	C	PRO	A	365	18.589	13.631	12.808	1.00 54.14	A
ATOM	2825	O	PRO	A	365	19.115	13.355	13.887	1.00 54.14	A
ATOM	2826	N	VAL	A	366	18.977	14.656	12.058	1.00 60.13	A
ATOM	2827	CA	VAL	A	366	20.048	15.537	12.487	1.00 60.13	A
ATOM	2828	CB	VAL	A	366	20.995	15.884	11.321	1.00 76.49	A
ATOM	2829	CG1	VAL	A	366	22.142	16.744	11.824	1.00 76.49	A
ATOM	2830	CG2	VAL	A	366	21.521	14.608	10.682	1.00 76.49	A
ATOM	2831	C	VAL	A	366	19.456	16.825	13.036	1.00 60.13	A
ATOM	2832	O	VAL	A	366	18.631	17.471	12.389	1.00 60.13	A
ATOM	2833	N	ILE	A	367	19.887	17.188	14.237	1.00 56.80	A
ATOM	2834	CA	ILE	A	367	19.416	18.392	14.892	1.00 56.80	A
ATOM	2835	CB	ILE	A	367	18.727	18.042	16.233	1.00 56.93	A
ATOM	2836	CG2	ILE	A	367	18.512	19.289	17.077	1.00 56.93	A

FIGURE 25 CON'T

ATOM	2837	CG1	ILE	A	367	17.397	17.341	15.952	1.00	56.93	A
ATOM	2838	CD1	ILE	A	367	16.394	18.190	15.180	1.00	56.93	A
ATOM	2839	C	ILE	A	367	20.614	19.294	15.133	1.00	56.80	A
ATOM	2840	O	ILE	A	367	21.596	18.885	15.745	1.00	56.80	A
ATOM	2841	N	LEU	A	368	20.537	20.523	14.642	1.00	55.93	A
ATOM	2842	CA	LEU	A	368	21.632	21.467	14.814	1.00	55.93	A
ATOM	2843	CB	LEU	A	368	21.925	22.170	13.484	1.00	64.80	A
ATOM	2844	CG	LEU	A	368	23.235	22.948	13.340	1.00	64.80	A
ATOM	2845	CD1	LEU	A	368	23.180	24.216	14.165	1.00	64.80	A
ATOM	2846	CD2	LEU	A	368	24.404	22.066	13.767	1.00	64.80	A
ATOM	2847	C	LEU	A	368	21.249	22.479	15.886	1.00	55.93	A
ATOM	2848	O	LEU	A	368	20.405	23.349	15.664	1.00	55.93	A
ATOM	2849	N	PRO	A	369	21.871	22.375	17.070	1.00	54.36	A
ATOM	2850	CD	PRO	A	369	22.843	21.326	17.416	1.00	55.34	A
ATOM	2851	CA	PRO	A	369	21.630	23.254	18.221	1.00	54.36	A
ATOM	2852	CB	PRO	A	369	22.542	22.668	19.302	1.00	55.34	A
ATOM	2853	CG	PRO	A	369	22.670	21.230	18.906	1.00	55.34	A
ATOM	2854	C	PRO	A	369	21.928	24.738	17.978	1.00	54.36	A
ATOM	2855	O	PRO	A	369	22.768	25.099	17.148	1.00	54.36	A
ATOM	2856	N	TYR	A	370	21.235	25.593	18.717	1.00	56.23	A
ATOM	2857	CA	TYR	A	370	21.439	27.027	18.606	1.00	56.23	A
ATOM	2858	CB	TYR	A	370	20.132	27.767	18.899	1.00	65.92	A
ATOM	2859	CG	TYR	A	370	19.095	27.540	17.824	1.00	65.92	A
ATOM	2860	CD1	TYR	A	370	19.116	28.281	16.638	1.00	65.92	A
ATOM	2861	CE1	TYR	A	370	18.216	28.016	15.607	1.00	65.92	A
ATOM	2862	CD2	TYR	A	370	18.143	26.530	17.952	1.00	65.92	A
ATOM	2863	CE2	TYR	A	370	17.244	26.254	16.929	1.00	65.92	A
ATOM	2864	CZ	TYR	A	370	17.286	26.999	15.758	1.00	65.92	A
ATOM	2865	OH	TYR	A	370	16.409	26.712	14.741	1.00	65.92	A
ATOM	2866	C	TYR	A	370	22.514	27.408	19.612	1.00	56.23	A
ATOM	2867	O	TYR	A	370	23.215	28.404	19.439	1.00	56.23	A
ATOM	2868	N	GLU	A	371	22.633	26.594	20.661	1.00	62.81	A
ATOM	2869	CA	GLU	A	371	23.626	26.800	21.713	1.00	62.81	A
ATOM	2870	CB	GLU	A	371	23.072	27.693	22.829	1.00	68.13	A
ATOM	2871	CG	GLU	A	371	22.935	29.166	22.486	1.00	68.13	A
ATOM	2872	CD	GLU	A	371	22.631	30.018	23.714	1.00	68.13	A
ATOM	2873	OE1	GLU	A	371	23.351	29.875	24.724	1.00	68.13	A
ATOM	2874	OE2	GLU	A	371	21.683	30.830	23.673	1.00	68.13	A
ATOM	2875	C	GLU	A	371	24.045	25.466	22.325	1.00	62.81	A
ATOM	2876	O	GLU	A	371	23.224	24.562	22.500	1.00	62.81	A
ATOM	2877	N	VAL	A	372	25.329	25.351	22.647	1.00	53.69	A
ATOM	2878	CA	VAL	A	372	25.868	24.145	23.262	1.00	53.69	A
ATOM	2879	CB	VAL	A	372	26.710	23.327	22.262	1.00	45.98	A
ATOM	2880	CG1	VAL	A	372	27.399	22.165	22.975	1.00	45.98	A
ATOM	2881	CG2	VAL	A	372	25.823	22.800	21.152	1.00	45.98	A
ATOM	2882	C	VAL	A	372	26.757	24.580	24.419	1.00	53.69	A
ATOM	2883	O	VAL	A	372	27.671	25.385	24.232	1.00	53.69	A
ATOM	2884	N	PRO	A	373	26.492	24.067	25.636	1.00	56.69	A
ATOM	2885	CD	PRO	A	373	25.482	23.052	25.996	1.00	56.28	A
ATOM	2886	CA	PRO	A	373	27.304	24.431	26.803	1.00	56.69	A
ATOM	2887	CB	PRO	A	373	26.997	23.308	27.789	1.00	56.28	A
ATOM	2888	CG	PRO	A	373	25.545	23.047	27.516	1.00	56.28	A
ATOM	2889	C	PRO	A	373	28.783	24.491	26.419	1.00	56.69	A
ATOM	2890	O	PRO	A	373	29.285	23.612	25.716	1.00	56.69	A
ATOM	2891	N	GLU	A	374	29.474	25.534	26.861	1.00	69.16	A
ATOM	2892	CA	GLU	A	374	30.883	25.675	26.525	1.00	69.16	A

FIGURE 25 CON'T

```
ATOM   2893  CB  GLU A 374      31.386  27.050  26.977  1.00135.63      A
ATOM   2894  CG  GLU A 374      30.655  28.197  26.279  1.00135.63      A
ATOM   2895  CD  GLU A 374      31.132  29.570  26.712  1.00135.63      A
ATOM   2896  OE1 GLU A 374      31.019  29.893  27.913  1.00135.63      A
ATOM   2897  OE2 GLU A 374      31.616  30.331  25.848  1.00135.63      A
ATOM   2898  C   GLU A 374      31.706  24.545  27.143  1.00 69.16      A
ATOM   2899  O   GLU A 374      32.843  24.295  26.743  1.00 69.16      A
ATOM   2900  N   LYS A 375      31.105  23.847  28.102  1.00 88.08      A
ATOM   2901  CA  LYS A 375      31.758  22.734  28.777  1.00 88.08      A
ATOM   2902  CB  LYS A 375      30.815  22.126  29.814  1.00112.71      A
ATOM   2903  CG  LYS A 375      31.323  20.817  30.386  1.00112.71      A
ATOM   2904  CD  LYS A 375      30.267  20.112  31.208  1.00112.71      A
ATOM   2905  CE  LYS A 375      30.738  18.723  31.593  1.00112.71      A
ATOM   2906  NZ  LYS A 375      31.981  18.761  32.414  1.00112.71      A
ATOM   2907  C   LYS A 375      32.205  21.638  27.813  1.00 88.08      A
ATOM   2908  O   LYS A 375      33.281  21.061  27.974  1.00 88.08      A
ATOM   2909  N   PHE A 376      31.373  21.349  26.817  1.00 74.38      A
ATOM   2910  CA  PHE A 376      31.669  20.305  25.840  1.00 74.38      A
ATOM   2911  CB  PHE A 376      30.433  20.041  24.972  1.00 57.91      A
ATOM   2912  CG  PHE A 376      29.296  19.419  25.719  1.00 57.91      A
ATOM   2913  CD1 PHE A 376      29.330  18.076  26.065  1.00 57.91      A
ATOM   2914  CD2 PHE A 376      28.210  20.184  26.119  1.00 57.91      A
ATOM   2915  CE1 PHE A 376      28.297  17.503  26.803  1.00 57.91      A
ATOM   2916  CE2 PHE A 376      27.172  19.621  26.858  1.00 57.91      A
ATOM   2917  CZ  PHE A 376      27.217  18.278  27.201  1.00 57.91      A
ATOM   2918  C   PHE A 376      32.870  20.601  24.942  1.00 74.38      A
ATOM   2919  O   PHE A 376      33.449  19.686  24.353  1.00 74.38      A
ATOM   2920  N   ARG A 377      33.240  21.874  24.837  1.00100.66      A
ATOM   2921  CA  ARG A 377      34.373  22.267  24.004  1.00100.66      A
ATOM   2922  CB  ARG A 377      34.532  23.789  24.013  1.00127.11      A
ATOM   2923  CG  ARG A 377      33.342  24.546  23.444  1.00127.11      A
ATOM   2924  CD  ARG A 377      33.595  26.047  23.462  1.00127.11      A
ATOM   2925  NE  ARG A 377      32.486  26.809  22.893  1.00127.11      A
ATOM   2926  CZ  ARG A 377      32.472  28.134  22.780  1.00127.11      A
ATOM   2927  NH1 ARG A 377      33.508  28.849  23.198  1.00127.11      A
ATOM   2928  NH2 ARG A 377      31.423  28.747  22.248  1.00127.11      A
ATOM   2929  C   ARG A 377      35.676  21.613  24.466  1.00100.66      A
ATOM   2930  O   ARG A 377      36.444  21.101  23.651  1.00100.66      A
ATOM   2931  N   LYS A 378      35.914  21.626  25.775  1.00114.97      A
ATOM   2932  CA  LYS A 378      37.127  21.048  26.351  1.00114.97      A
ATOM   2933  CB  LYS A 378      37.396  21.667  27.728  1.00131.02      A
ATOM   2934  CG  LYS A 378      38.739  21.289  28.345  1.00131.02      A
ATOM   2935  CD  LYS A 378      39.908  21.866  27.553  1.00131.02      A
ATOM   2936  CE  LYS A 378      41.244  21.539  28.211  1.00131.02      A
ATOM   2937  NZ  LYS A 378      42.406  22.107  27.467  1.00131.02      A
ATOM   2938  C   LYS A 378      37.061  19.523  26.482  1.00114.97      A
ATOM   2939  O   LYS A 378      37.970  18.821  26.036  1.00114.97      A
ATOM   2940  N   ILE A 379      35.988  19.027  27.097  1.00 92.81      A
ATOM   2941  CA  ILE A 379      35.775  17.591  27.314  1.00 92.81      A
ATOM   2942  CB  ILE A 379      34.265  17.267  27.384  1.00 81.77      A
ATOM   2943  CG2 ILE A 379      34.051  15.774  27.574  1.00 81.77      A
ATOM   2944  CG1 ILE A 379      33.627  18.044  28.534  1.00 81.77      A
ATOM   2945  CD1 ILE A 379      32.126  17.890  28.612  1.00 81.77      A
ATOM   2946  C   ILE A 379      36.410  16.690  26.254  1.00 92.81      A
ATOM   2947  O   ILE A 379      36.134  16.828  25.062  1.00 92.81      A
ATOM   2948  N   ARG A 380      37.261  15.767  26.698  1.00111.06      A
ATOM   2949  CA  ARG A 380      37.930  14.842  25.789  1.00111.06      A
```

FIGURE 25 CON'T

```
ATOM   2950  CB  ARG A 380      39.002  14.035  26.530  1.00115.46      A
ATOM   2951  CG  ARG A 380      40.322  14.765  26.730  1.00115.46      A
ATOM   2952  CD  ARG A 380      41.429  13.795  27.137  1.00115.46      A
ATOM   2953  NE  ARG A 380      42.750  14.421  27.104  1.00115.46      A
ATOM   2954  CZ  ARG A 380      43.889  13.778  27.343  1.00115.46      A
ATOM   2955  NH1 ARG A 380      43.875  12.484  27.633  1.00115.46      A
ATOM   2956  NH2 ARG A 380      45.045  14.428  27.289  1.00115.46      A
ATOM   2957  C   ARG A 380      36.937  13.883  25.142  1.00111.06      A
ATOM   2958  O   ARG A 380      36.373  14.174  24.087  1.00111.06      A
ATOM   2959  N   GLU A 381      36.735  12.736  25.782  1.00 81.80      A
ATOM   2960  CA  GLU A 381      35.814  11.722  25.286  1.00 81.80      A
ATOM   2961  CB  GLU A 381      36.499  10.359  25.238  1.00109.22      A
ATOM   2962  CG  GLU A 381      36.798   9.811  26.627  1.00109.22      A
ATOM   2963  CD  GLU A 381      37.160   8.342  26.620  1.00109.22      A
ATOM   2964  OE1 GLU A 381      36.351   7.534  26.118  1.00109.22      A
ATOM   2965  OE2 GLU A 381      38.250   7.995  27.124  1.00109.22      A
ATOM   2966  C   GLU A 381      34.619  11.611  26.226  1.00 81.80      A
ATOM   2967  O   GLU A 381      34.671  12.036  27.380  1.00 81.80      A
ATOM   2968  N   ILE A 382      33.541  11.030  25.722  1.00 54.73      A
ATOM   2969  CA  ILE A 382      32.351  10.824  26.529  1.00 54.73      A
ATOM   2970  CB  ILE A 382      31.170  11.684  26.028  1.00 57.74      A
ATOM   2971  CG2 ILE A 382      29.906  11.352  26.817  1.00 57.74      A

ATOM   2972  CG1 ILE A 382      31.511  13.167  26.185  1.00 57.74      A
ATOM   2973  CD1 ILE A 382      30.405  14.104  25.745  1.00 57.74      A
ATOM   2974  C   ILE A 382      31.995   9.345  26.427  1.00 54.73      A
ATOM   2975  O   ILE A 382      31.445   8.903  25.428  1.00 54.73      A
ATOM   2976  N   PRO A 383      32.350   8.551  27.450  1.00 43.50      A
ATOM   2977  CD  PRO A 383      33.094   8.915  28.670  1.00 50.24      A
ATOM   2978  CA  PRO A 383      32.041   7.116  27.432  1.00 43.50      A
ATOM   2979  CB  PRO A 383      32.477   6.654  28.821  1.00 50.24      A
ATOM   2980  CG  PRO A 383      33.625   7.577  29.130  1.00 50.24      A
ATOM   2981  C   PRO A 383      30.538   6.898  27.191  1.00 43.50      A
ATOM   2982  O   PRO A 383      29.705   7.629  27.729  1.00 43.50      A
ATOM   2983  N   MSE A 384      30.214   5.884  26.393  1.00 58.26      A
ATOM   2984  CA  MSE A 384      28.830   5.562  26.050  1.00 58.26      A
ATOM   2985  CB  MSE A 384      28.656   5.580  24.531  1.00174.03      A
ATOM   2986  CG  MSE A 384      27.298   6.058  24.071  1.00174.03      A
ATOM   2987  SE  MSE A 384      27.115   7.952  24.377  1.00174.03      A
ATOM   2988  CE  MSE A 384      27.699   8.580  22.656  1.00174.03      A
ATOM   2989  C   MSE A 384      28.429   4.188  26.577  1.00 58.26      A
ATOM   2990  O   MSE A 384      29.040   3.182  26.231  1.00 58.26      A
ATOM   2991  N   PHE A 385      27.387   4.144  27.399  1.00 44.08      A
ATOM   2992  CA  PHE A 385      26.925   2.883  27.963  1.00 44.08      A
ATOM   2993  CB  PHE A 385      26.897   2.981  29.487  1.00 43.39      A
ATOM   2994  CG  PHE A 385      28.220   3.286  30.093  1.00 43.39      A
ATOM   2995  CD1 PHE A 385      29.180   2.279  30.252  1.00 43.39      A
ATOM   2996  CD2 PHE A 385      28.522   4.579  30.504  1.00 43.39      A
ATOM   2997  CE1 PHE A 385      30.423   2.563  30.813  1.00 43.39      A
ATOM   2998  CE2 PHE A 385      29.758   4.878  31.068  1.00 43.39      A
ATOM   2999  CZ  PHE A 385      30.715   3.865  31.223  1.00 43.39      A
ATOM   3000  C   PHE A 385      25.539   2.483  27.476  1.00 44.08      A
ATOM   3001  O   PHE A 385      24.614   3.298  27.478  1.00 44.08      A
ATOM   3002  N   ILE A 386      25.417   1.225  27.061  1.00 38.93      A
ATOM   3003  CA  ILE A 386      24.159   0.638  26.606  1.00 38.93      A
ATOM   3004  CB  ILE A 386      24.322  -0.164  25.295  1.00 45.03      A
ATOM   3005  CG2 ILE A 386      23.020  -0.893  24.961  1.00 45.03      A
```

FIGURE 25 CON'T

```
ATOM   3006  CG1 ILE A 386      24.791   0.759  24.164  1.00 45.03      A
ATOM   3007  CD1 ILE A 386      24.047   2.033  24.095  1.00 45.03      A
ATOM   3008  C   ILE A 386      23.805  -0.350  27.701  1.00 38.93      A
ATOM   3009  O   ILE A 386      24.476  -1.365  27.852  1.00 38.93      A
ATOM   3010  N   ILE A 387      22.760  -0.060  28.464  1.00 36.29      A
ATOM   3011  CA  ILE A 387      22.356  -0.925  29.568  1.00 36.29      A
ATOM   3012  CB  ILE A 387      22.175  -0.086  30.840  1.00 38.17      A
ATOM   3013  CG2 ILE A 387      21.760  -0.979  32.023  1.00 38.17      A
ATOM   3014  CG1 ILE A 387      23.499   0.633  31.130  1.00 38.17      A
ATOM   3015  CD1 ILE A 387      23.485   1.568  32.316  1.00 38.17      A
ATOM   3016  C   ILE A 387      21.081  -1.681  29.223  1.00 36.29      A
ATOM   3017  O   ILE A 387      20.003  -1.092  29.095  1.00 36.29      A
ATOM   3018  N   LEU A 388      21.215  -2.996  29.090  1.00 43.27      A
ATOM   3019  CA  LEU A 388      20.106  -3.850  28.703  1.00 43.27      A
ATOM   3020  CB  LEU A 388      20.537  -4.738  27.538  1.00 38.32      A
ATOM   3021  CG  LEU A 388      21.153  -4.011  26.333  1.00 38.32      A
ATOM   3022  CD1 LEU A 388      21.640  -5.036  25.277  1.00 38.32      A
ATOM   3023  CD2 LEU A 388      20.109  -3.058  25.752  1.00 38.32      A
ATOM   3024  C   LEU A 388      19.516  -4.728  29.796  1.00 43.27      A
ATOM   3025  O   LEU A 388      20.197  -5.563  30.389  1.00 43.27      A
ATOM   3026  N   ASP A 389      18.231  -4.538  30.042  1.00 49.60      A
ATOM   3027  CA  ASP A 389      17.533  -5.324  31.030  1.00 49.60      A
ATOM   3028  CB  ASP A 389      16.119  -4.790  31.185  1.00 45.78      A
ATOM   3029  CG  ASP A 389      15.357  -5.504  32.251  1.00 45.78      A
ATOM   3030  OD1 ASP A 389      15.977  -6.321  32.960  1.00 45.78      A
ATOM   3031  OD2 ASP A 389      14.144  -5.242  32.386  1.00 45.78      A
ATOM   3032  C   ASP A 389      17.512  -6.766  30.516  1.00 49.60      A
ATOM   3033  O   ASP A 389      16.870  -7.055  29.502  1.00 49.60      A
ATOM   3034  N   SER A 390      18.219  -7.659  31.208  1.00 56.04      A
ATOM   3035  CA  SER A 390      18.299  -9.056  30.794  1.00 56.04      A
ATOM   3036  CB  SER A 390      19.178  -9.861  31.757  1.00 40.57      A
ATOM   3037  OG  SER A 390      18.614  -9.872  33.058  1.00 40.57      A
ATOM   3038  C   SER A 390      16.932  -9.713  30.692  1.00 56.04      A
ATOM   3039  O   SER A 390      16.796 -10.764  30.073  1.00 56.04      A
ATOM   3040  N   GLY A 391      15.925  -9.098  31.302  1.00 60.83      A
ATOM   3041  CA  GLY A 391      14.585  -9.651  31.236  1.00 60.83      A
ATOM   3042  C   GLY A 391      13.949  -9.514  29.859  1.00 60.83      A
ATOM   3043  O   GLY A 391      13.041 -10.271  29.519  1.00 60.83      A
ATOM   3044  N   LEU A 392      14.420  -8.559  29.061  1.00 55.40      A
ATOM   3045  CA  LEU A 392      13.868  -8.345  27.724  1.00 55.40      A
ATOM   3046  CB  LEU A 392      14.343  -7.006  27.154  1.00 36.97      A
ATOM   3047  CG  LEU A 392      14.002  -5.708  27.896  1.00 36.97      A
ATOM   3048  CD1 LEU A 392      14.885  -4.596  27.350  1.00 36.97      A
ATOM   3049  CD2 LEU A 392      12.506  -5.368  27.742  1.00 36.97      A
ATOM   3050  C   LEU A 392      14.281  -9.454  26.755  1.00 55.40      A
ATOM   3051  O   LEU A 392      15.410  -9.947  26.808  1.00 55.40      A
ATOM   3052  N   LEU A 393      13.364  -9.839  25.868  1.00 60.39      A
ATOM   3053  CA  LEU A 393      13.661 -10.867  24.874  1.00 60.39      A
ATOM   3054  CB  LEU A 393      12.482 -11.044  23.914  1.00 55.91      A
ATOM   3055  CG  LEU A 393      11.209 -11.658  24.505  1.00 55.91      A
ATOM   3056  CD1 LEU A 393      10.057 -11.490  23.528  1.00 55.91      A
ATOM   3057  CD2 LEU A 393      11.447 -13.125  24.823  1.00 55.91      A
ATOM   3058  C   LEU A 393      14.891 -10.427  24.094  1.00 60.39      A
ATOM   3059  O   LEU A 393      15.143  -9.228  23.938  1.00 60.39      A
ATOM   3060  N   ALA A 394      15.658 -11.395  23.608  1.00 60.28      A
ATOM   3061  CA  ALA A 394      16.865 -11.101  22.847  1.00 60.28      A
ATOM   3062  CB  ALA A 394      17.460 -12.394  22.303  1.00 64.50      A
```

FIGURE 25 CON'T

```
ATOM   3063  C   ALA A 394      16.635 -10.112  21.701  1.00 60.28      A
ATOM   3064  O   ALA A 394      17.414  -9.177  21.523  1.00 60.28      A
ATOM   3065  N   ASP A 395      15.570 -10.317  20.929  1.00 55.46      A
ATOM   3066  CA  ASP A 395      15.279  -9.443  19.796  1.00 55.46      A
ATOM   3067  CB  ASP A 395      14.128 -10.027  18.949  1.00 69.32      A
ATOM   3068  CG  ASP A 395      12.777  -9.939  19.632  1.00 69.32      A
ATOM   3069  OD1 ASP A 395      12.217  -8.825  19.709  1.00 69.32      A
ATOM   3070  OD2 ASP A 395      12.264 -10.988  20.085  1.00 69.32      A
ATOM   3071  C   ASP A 395      14.985  -7.996  20.200  1.00 55.46      A
ATOM   3072  O   ASP A 395      15.308  -7.065  19.466  1.00 55.46      A
ATOM   3073  N   ILE A 396      14.366  -7.805  21.359  1.00 47.75      A
ATOM   3074  CA  ILE A 396      14.087  -6.457  21.835  1.00 47.75      A
ATOM   3075  CB  ILE A 396      13.179  -6.472  23.073  1.00 47.69      A
ATOM   3076  CG2 ILE A 396      12.956  -5.042  23.554  1.00 47.69      A
ATOM   3077  CG1 ILE A 396      11.849  -7.161  22.746  1.00 47.69      A
ATOM   3078  CD1 ILE A 396      11.006  -6.430  21.721  1.00 47.69      A
ATOM   3079  C   ILE A 396      15.439  -5.825  22.220  1.00 47.75      A
ATOM   3080  O   ILE A 396      15.713  -4.664  21.906  1.00 47.75      A
ATOM   3081  N   GLN A 397      16.280  -6.611  22.888  1.00 48.02      A
ATOM   3082  CA  GLN A 397      17.603  -6.148  23.295  1.00 48.02      A
ATOM   3083  CB  GLN A 397      18.369  -7.256  24.029  1.00 48.61      A
ATOM   3084  CG  GLN A 397      17.952  -7.448  25.475  1.00 48.61      A
ATOM   3085  CD  GLN A 397      18.797  -8.491  26.195  1.00 48.61      A
ATOM   3086  OE1 GLN A 397      20.023  -8.516  26.070  1.00 48.61      A
ATOM   3087  NE2 GLN A 397      18.147  -9.346  26.957  1.00 48.61      A
ATOM   3088  C   GLN A 397      18.415  -5.677  22.095  1.00 48.02      A
ATOM   3089  O   GLN A 397      19.048  -4.630  22.155  1.00 48.02      A
ATOM   3090  N   ASN A 398      18.396  -6.442  21.004  1.00 58.81      A
ATOM   3091  CA  ASN A 398      19.147  -6.057  19.807  1.00 58.81      A
ATOM   3092  CB  ASN A 398      19.142  -7.189  18.779  1.00110.12      A
ATOM   3093  CG  ASN A 398      19.876  -8.418  19.268  1.00110.12      A
ATOM   3094  OD1 ASN A 398      21.016  -8.331  19.726  1.00110.12      A
ATOM   3095  ND2 ASN A 398      19.230  -9.575  19.168  1.00110.12      A
ATOM   3096  C   ASN A 398      18.578  -4.792  19.176  1.00 58.81      A
ATOM   3097  O   ASN A 398      19.320  -3.925  18.714  1.00 58.81      A
ATOM   3098  N   PHE A 399      17.256  -4.698  19.147  1.00 52.07      A
ATOM   3099  CA  PHE A 399      16.583  -3.530  18.586  1.00 52.07      A

ATOM   3100  CB  PHE A 399      15.068  -3.680  18.757  1.00 70.91      A
ATOM   3101  CG  PHE A 399      14.275  -2.502  18.267  1.00 70.91      A
ATOM   3102  CD1 PHE A 399      14.162  -2.237  16.908  1.00 70.91      A
ATOM   3103  CD2 PHE A 399      13.625  -1.664  19.169  1.00 70.91      A
ATOM   3104  CE1 PHE A 399      13.411  -1.156  16.451  1.00 70.91      A
ATOM   3105  CE2 PHE A 399      12.871  -0.579  18.721  1.00 70.91      A
ATOM   3106  CZ  PHE A 399      12.765  -0.327  17.358  1.00 70.91      A
ATOM   3107  C   PHE A 399      17.070  -2.270  19.312  1.00 52.07      A
ATOM   3108  O   PHE A 399      17.555  -1.324  18.686  1.00 52.07      A
ATOM   3109  N   ALA A 400      16.940  -2.276  20.637  1.00 49.37      A
ATOM   3110  CA  ALA A 400      17.357  -1.149  21.471  1.00 49.37      A
ATOM   3111  CB  ALA A 400      17.125  -1.478  22.945  1.00 38.64      A
ATOM   3112  C   ALA A 400      18.811  -0.716  21.260  1.00 49.37      A
ATOM   3113  O   ALA A 400      19.081   0.468  21.040  1.00 49.37      A
ATOM   3114  N   THR A 401      19.754  -1.651  21.315  1.00 50.15      A
ATOM   3115  CA  THR A 401      21.140  -1.245  21.140  1.00 50.15      A
ATOM   3116  CB  THR A 401      22.139  -2.419  21.318  1.00 55.89      A
ATOM   3117  OG1 THR A 401      22.499  -2.940  20.038  1.00 55.89      A
ATOM   3118  CG2 THR A 401      21.545  -3.517  22.159  1.00 55.89      A
```

FIGURE 25 CON'T

```
ATOM   3119  C   THR A 401      21.328  -0.608  19.759  1.00 50.15      A
ATOM   3120  O   THR A 401      22.097   0.349  19.609  1.00 50.15      A
ATOM   3121  N   ASN A 402      20.626  -1.118  18.747  1.00 54.40      A
ATOM   3122  CA  ASN A 402      20.755  -0.525  17.421  1.00 54.40      A
ATOM   3123  CB  ASN A 402      20.121  -1.416  16.345  1.00 77.17      A
ATOM   3124  CG  ASN A 402      20.976  -2.635  16.018  1.00 77.17      A
ATOM   3125  OD1 ASN A 402      22.208  -2.583  16.088  1.00 77.17      A
ATOM   3126  ND2 ASN A 402      20.327  -3.732  15.640  1.00 77.17      A
ATOM   3127  C   ASN A 402      20.132   0.868  17.407  1.00 54.40      A
ATOM   3128  O   ASN A 402      20.646   1.769  16.742  1.00 54.40      A
ATOM   3129  N   GLU A 403      19.031   1.050  18.135  1.00 49.70      A
ATOM   3130  CA  GLU A 403      18.398   2.367  18.205  1.00 49.70      A
ATOM   3131  CB  GLU A 403      17.073   2.321  18.985  1.00 49.89      A
ATOM   3132  CG  GLU A 403      15.827   2.069  18.156  1.00 49.89      A
ATOM   3133  CD  GLU A 403      15.624   3.095  17.044  1.00 49.89      A
ATOM   3134  OE1 GLU A 403      15.560   4.317  17.328  1.00 49.89      A
ATOM   3135  OE2 GLU A 403      15.527   2.661  15.877  1.00 49.89      A
ATOM   3136  C   GLU A 403      19.338   3.325  18.928  1.00 49.70      A
ATOM   3137  O   GLU A 403      19.517   4.468  18.514  1.00 49.70      A
ATOM   3138  N   PHE A 404      19.930   2.854  20.022  1.00 37.64      A
ATOM   3139  CA  PHE A 404      20.839   3.694  20.808  1.00 37.64      A
ATOM   3140  CB  PHE A 404      21.262   2.980  22.108  1.00 42.21      A
ATOM   3141  CG  PHE A 404      20.122   2.683  23.050  1.00 42.21      A
ATOM   3142  CD1 PHE A 404      19.042   3.555  23.162  1.00 42.21      A
ATOM   3143  CD2 PHE A 404      20.170   1.571  23.889  1.00 42.21      A
ATOM   3144  CE1 PHE A 404      18.029   3.330  24.100  1.00 42.21      A
ATOM   3145  CE2 PHE A 404      19.163   1.338  24.831  1.00 42.21      A
ATOM   3146  CZ  PHE A 404      18.093   2.219  24.937  1.00 42.21      A
ATOM   3147  C   PHE A 404      22.083   4.070  20.013  1.00 37.64      A
ATOM   3148  O   PHE A 404      22.570   5.186  20.111  1.00 37.64      A
ATOM   3149  N   ARG A 405      22.607   3.122  19.243  1.00 47.85      A
ATOM   3150  CA  ARG A 405      23.791   3.376  18.432  1.00 47.85      A
ATOM   3151  CB  ARG A 405      24.184   2.114  17.666  1.00 54.53      A
ATOM   3152  CG  ARG A 405      24.918   1.121  18.537  1.00 54.53      A
ATOM   3153  CD  ARG A 405      25.170  -0.193  17.835  1.00 54.53      A
ATOM   3154  NE  ARG A 405      26.055  -1.022  18.642  1.00 54.53      A
ATOM   3155  CZ  ARG A 405      26.160  -2.339  18.536  1.00 54.53      A
ATOM   3156  NH1 ARG A 405      25.430  -2.998  17.653  1.00 54.53      A
ATOM   3157  NH2 ARG A 405      27.001  -2.997  19.322  1.00 54.53      A
ATOM   3158  C   ARG A 405      23.562   4.524  17.460  1.00 47.85      A
ATOM   3159  O   ARG A 405      24.430   5.370  17.276  1.00 47.85      A
ATOM   3160  N   GLU A 406      22.386   4.559  16.844  1.00 45.39      A
ATOM   3161  CA  GLU A 406      22.081   5.623  15.898  1.00 45.39      A
ATOM   3162  CB  GLU A 406      20.885   5.241  15.022  1.00 63.52      A
ATOM   3163  CG  GLU A 406      21.147   4.064  14.108  1.00 63.52      A
ATOM   3164  CD  GLU A 406      22.394   4.256  13.260  1.00 63.52      A
ATOM   3165  OE1 GLU A 406      22.572   5.354  12.687  1.00 63.52      A
ATOM   3166  OE2 GLU A 406      23.197   3.307  13.162  1.00 63.52      A
ATOM   3167  C   GLU A 406      21.791   6.920  16.628  1.00 45.39      A
ATOM   3168  O   GLU A 406      22.093   7.998  16.129  1.00 45.39      A
ATOM   3169  N   LEU A 407      21.204   6.819  17.817  1.00 51.19      A
ATOM   3170  CA  LEU A 407      20.896   8.015  18.586  1.00 51.19      A
ATOM   3171  CB  LEU A 407      20.106   7.651  19.844  1.00 55.82      A
ATOM   3172  CG  LEU A 407      19.425   8.803  20.586  1.00 55.82      A
ATOM   3173  CD1 LEU A 407      18.523   8.239  21.659  1.00 55.82      A
ATOM   3174  CD2 LEU A 407      20.457   9.721  21.194  1.00 55.82      A
ATOM   3175  C   LEU A 407      22.192   8.733  18.959  1.00 51.19      A
```

FIGURE 25 CON'T

```
ATOM   3176  O   LEU A 407      22.280   9.956  18.859  1.00 51.19      A
ATOM   3177  N   VAL A 408      23.204   7.982  19.379  1.00 54.33      A
ATOM   3178  CA  VAL A 408      24.465   8.614  19.747  1.00 54.33      A
ATOM   3179  CB  VAL A 408      25.446   7.612  20.411  1.00 69.32      A
ATOM   3180  CG1 VAL A 408      24.853   7.098  21.706  1.00 69.32      A
ATOM   3181  CG2 VAL A 408      25.749   6.460  19.468  1.00 69.32      A
ATOM   3182  C   VAL A 408      25.147   9.262  18.545  1.00 54.33      A
ATOM   3183  O   VAL A 408      25.741  10.334  18.670  1.00 54.33      A
ATOM   3184  N   LYS A 409      25.064   8.625  17.382  1.00 55.85      A
ATOM   3185  CA  LYS A 409      25.677   9.191  16.185  1.00 55.85      A
ATOM   3186  CB  LYS A 409      25.433   8.287  14.979  1.00 68.43      A
ATOM   3187  CG  LYS A 409      26.205   6.986  15.053  1.00 68.43      A
ATOM   3188  CD  LYS A 409      25.832   6.029  13.940  1.00 68.43      A
ATOM   3189  CE  LYS A 409      26.575   4.710  14.106  1.00 68.43      A
ATOM   3190  NZ  LYS A 409      26.108   3.662  13.151  1.00 68.43      A
ATOM   3191  C   LYS A 409      25.139  10.591  15.915  1.00 55.85      A
ATOM   3192  O   LYS A 409      25.917  11.531  15.766  1.00 55.85      A
ATOM   3193  N   SER A 410      23.817  10.748  15.868  1.00 59.15      A
ATOM   3194  CA  SER A 410      23.254  12.070  15.620  1.00 59.15      A
ATOM   3195  CB  SER A 410      21.739  11.995  15.413  1.00 72.56      A
ATOM   3196  OG  SER A 410      21.083  11.594  16.597  1.00 72.56      A
ATOM   3197  C   SER A 410      23.584  12.963  16.816  1.00 59.15      A
ATOM   3198  O   SER A 410      23.730  14.182  16.682  1.00 59.15      A
ATOM   3199  N   MSE A 411      23.695  12.344  17.985  1.00 63.76      A
ATOM   3200  CA  MSE A 411      24.044  13.059  19.207  1.00 63.76      A
ATOM   3201  CB  MSE A 411      24.321  12.058  20.327  1.00100.84      A
ATOM   3202  CG  MSE A 411      23.146  11.807  21.223  1.00100.84      A
ATOM   3203  SE  MSE A 411      22.889  13.373  22.260  1.00100.84      A
ATOM   3204  CE  MSE A 411      24.121  12.935  23.679  1.00100.84      A
ATOM   3205  C   MSE A 411      25.302  13.885  18.938  1.00 63.76      A
ATOM   3206  O   MSE A 411      25.502  14.956  19.514  1.00 63.76      A
ATOM   3207  N   TYR A 412      26.144  13.364  18.052  1.00 85.83      A
ATOM   3208  CA  TYR A 412      27.377  14.033  17.674  1.00 85.83      A
ATOM   3209  CB  TYR A 412      28.501  13.008  17.512  1.00113.02      A
ATOM   3210  CG  TYR A 412      28.851  12.306  18.805  1.00113.02      A
ATOM   3211  CD1 TYR A 412      29.215  13.036  19.935  1.00113.02      A
ATOM   3212  CE1 TYR A 412      29.534  12.401  21.133  1.00113.02      A
ATOM   3213  CD2 TYR A 412      28.815  10.915  18.903  1.00113.02      A
ATOM   3214  CE2 TYR A 412      29.133  10.268  20.099  1.00113.02      A
ATOM   3215  CZ  TYR A 412      29.492  11.020  21.210  1.00113.02      A
ATOM   3216  OH  TYR A 412      29.811  10.397  22.396  1.00113.02      A
ATOM   3217  C   TYR A 412      27.164  14.809  16.383  1.00 85.83      A
ATOM   3218  O   TYR A 412      27.591  14.390  15.304  1.00 85.83      A
ATOM   3219  N   TYR A 413      26.473  15.936  16.529  1.00 87.35      A
ATOM   3220  CA  TYR A 413      26.150  16.866  15.451  1.00 87.35      A
ATOM   3221  CB  TYR A 413      26.379  18.294  15.955  1.00 83.41      A
ATOM   3222  CG  TYR A 413      26.617  18.343  17.449  1.00 83.41      A
ATOM   3223  CD1 TYR A 413      25.598  18.009  18.344  1.00 83.41      A
ATOM   3224  CE1 TYR A 413      25.836  17.940  19.716  1.00 83.41      A
ATOM   3225  CD2 TYR A 413      27.887  18.624  17.968  1.00 83.41      A
ATOM   3226  CE2 TYR A 413      28.136  18.559  19.345  1.00 83.41      A
ATOM   3227  CZ  TYR A 413      27.102  18.210  20.209  1.00 83.41      A

ATOM   3228  OH  TYR A 413      27.329  18.094  21.560  1.00 83.41      A
ATOM   3229  C   TYR A 413      26.966  16.625  14.180  1.00 87.35      A
ATOM   3230  O   TYR A 413      26.641  15.750  13.375  1.00 87.35      A
ATOM   3231  N   GLU A 443      32.228   2.350  23.459  1.00 66.73      A
```

FIGURE 25 CON'T

```
ATOM   3232  CA  GLU A 443      30.888   1.809  23.680  1.00 66.73      A
ATOM   3233  CB  GLU A 443      30.221   1.471  22.348  1.00 80.66      A
ATOM   3234  CG  GLU A 443      28.779   0.997  22.488  1.00 80.66      A
ATOM   3235  CD  GLU A 443      28.366   0.036  21.385  1.00 80.66      A
ATOM   3236  OE1 GLU A 443      28.796  -1.137  21.427  1.00 80.66      A
ATOM   3237  OE2 GLU A 443      27.619   0.452  20.474  1.00 80.66      A
ATOM   3238  C   GLU A 443      30.938   0.548  24.537  1.00 66.73      A
ATOM   3239  O   GLU A 443      31.601  -0.428  24.186  1.00 66.73      A
ATOM   3240  N   LYS A 444      30.229   0.560  25.656  1.00 47.77      A
ATOM   3241  CA  LYS A 444      30.225  -0.600  26.532  1.00 47.77      A
ATOM   3242  CB  LYS A 444      30.852  -0.244  27.885  1.00 86.81      A
ATOM   3243  CG  LYS A 444      31.656  -1.376  28.528  1.00 86.81      A
ATOM   3244  CD  LYS A 444      30.787  -2.580  28.867  1.00 86.81      A
ATOM   3245  CE  LYS A 444      31.609  -3.762  29.396  1.00 86.81      A
ATOM   3246  NZ  LYS A 444      32.471  -4.435  28.367  1.00 86.81      A
ATOM   3247  C   LYS A 444      28.798  -1.084  26.722  1.00 47.77      A
ATOM   3248  O   LYS A 444      27.926  -0.317  27.142  1.00 47.77      A
ATOM   3249  N   VAL A 445      28.559  -2.353  26.398  1.00 48.00      A
ATOM   3250  CA  VAL A 445      27.238  -2.948  26.543  1.00 48.00      A
ATOM   3251  CB  VAL A 445      26.908  -3.893  25.375  1.00 44.91      A
ATOM   3252  CG1 VAL A 445      25.528  -4.525  25.593  1.00 44.91      A
ATOM   3253  CG2 VAL A 445      26.935  -3.125  24.060  1.00 44.91      A
ATOM   3254  C   VAL A 445      27.148  -3.744  27.839  1.00 48.00      A
ATOM   3255  O   VAL A 445      27.938  -4.663  28.079  1.00 48.00      A
ATOM   3256  N   ILE A 446      26.185  -3.391  28.680  1.00 43.39      A
ATOM   3257  CA  ILE A 446      26.018  -4.092  29.934  1.00 43.39      A
ATOM   3258  CB  ILE A 446      26.253  -3.140  31.110  1.00 50.34      A
ATOM   3259  CG2 ILE A 446      25.991  -3.850  32.426  1.00 50.34      A
ATOM   3260  CG1 ILE A 446      27.698  -2.632  31.059  1.00 50.34      A
ATOM   3261  CD1 ILE A 446      27.976  -1.466  31.997  1.00 50.34      A
ATOM   3262  C   ILE A 446      24.628  -4.705  30.000  1.00 43.39      A
ATOM   3263  O   ILE A 446      23.624  -4.023  29.791  1.00 43.39      A
ATOM   3264  N   THR A 447      24.575  -5.999  30.285  1.00 45.08      A
ATOM   3265  CA  THR A 447      23.308  -6.715  30.370  1.00 45.08      A
ATOM   3266  CB  THR A 447      23.246  -7.840  29.316  1.00 46.71      A
ATOM   3267  OG1 THR A 447      23.499  -7.292  28.015  1.00 46.71      A
ATOM   3268  CG2 THR A 447      21.864  -8.513  29.324  1.00 46.71      A
ATOM   3269  C   THR A 447      23.117  -7.338  31.750  1.00 45.08      A
ATOM   3270  O   THR A 447      23.868  -8.222  32.133  1.00 45.08      A
ATOM   3271  N   GLU A 448      22.108  -6.888  32.490  1.00 47.89      A
ATOM   3272  CA  GLU A 448      21.841  -7.432  33.821  1.00 47.89      A
ATOM   3273  CB  GLU A 448      22.561  -6.614  34.902  1.00 48.58      A
ATOM   3274  CG  GLU A 448      24.084  -6.603  34.832  1.00 48.58      A
ATOM   3275  CD  GLU A 448      24.708  -7.982  34.994  1.00 48.58      A
ATOM   3276  OE1 GLU A 448      24.188  -8.803  35.790  1.00 48.58      A
ATOM   3277  OE2 GLU A 448      25.733  -8.240  34.330  1.00 48.58      A
ATOM   3278  C   GLU A 448      20.348  -7.434  34.122  1.00 47.89      A
ATOM   3279  O   GLU A 448      19.547  -6.879  33.366  1.00 47.89      A
ATOM   3280  N   ASP A 449      19.983  -8.053  35.240  1.00 50.32      A
ATOM   3281  CA  ASP A 449      18.595  -8.135  35.664  1.00 50.32      A
ATOM   3282  CB  ASP A 449      18.410  -9.334  36.598  1.00 66.69      A
ATOM   3283  CG  ASP A 449      16.969  -9.512  37.051  1.00 66.69      A
ATOM   3284  OD1 ASP A 449      16.116  -8.655  36.716  1.00 66.69      A
ATOM   3285  OD2 ASP A 449      16.697 -10.516  37.751  1.00 66.69      A
ATOM   3286  C   ASP A 449      18.195  -6.847  36.378  1.00 50.32      A
ATOM   3287  O   ASP A 449      18.244  -6.758  37.610  1.00 50.32      A
ATOM   3288  N   LEU A 450      17.791  -5.855  35.592  1.00 56.84      A
```

FIGURE 25 CON'T

```
ATOM   3289  CA  LEU A 450      17.391  -4.555  36.118  1.00 56.84      A
ATOM   3290  CB  LEU A 450      17.055  -3.610  34.958  1.00 46.05      A
ATOM   3291  CG  LEU A 450      18.164  -2.655  34.477  1.00 46.05      A
ATOM   3292  CD1 LEU A 450      19.552  -3.248  34.718  1.00 46.05      A
ATOM   3293  CD2 LEU A 450      17.941  -2.336  33.006  1.00 46.05      A
ATOM   3294  C   LEU A 450      16.229  -4.601  37.104  1.00 56.84      A
ATOM   3295  O   LEU A 450      15.948  -3.610  37.776  1.00 56.84      A
ATOM   3296  N   ASN A 451      15.554  -5.743  37.200  1.00 62.74      A
ATOM   3297  CA  ASN A 451      14.431  -5.851  38.123  1.00 62.74      A
ATOM   3298  CB  ASN A 451      13.287  -6.642  37.485  1.00 81.07      A
ATOM   3299  CG  ASN A 451      12.000  -6.545  38.282  1.00 81.07      A
ATOM   3300  OD1 ASN A 451      11.582  -5.451  38.675  1.00 81.07      A
ATOM   3301  ND2 ASN A 451      11.361  -7.686  38.521  1.00 81.07      A
ATOM   3302  C   ASN A 451      14.826  -6.488  39.450  1.00 62.74      A
ATOM   3303  O   ASN A 451      13.978  -6.951  40.212  1.00 62.74      A
ATOM   3304  N   SER A 452      16.123  -6.512  39.723  1.00 55.07      A
ATOM   3305  CA  SER A 452      16.626  -7.073  40.968  1.00 55.07      A
ATOM   3306  CB  SER A 452      17.250  -8.446  40.718  1.00 56.63      A
ATOM   3307  OG  SER A 452      18.399  -8.345  39.903  1.00 56.63      A
ATOM   3308  C   SER A 452      17.670  -6.111  41.526  1.00 55.07      A
ATOM   3309  O   SER A 452      18.385  -5.450  40.774  1.00 55.07      A
ATOM   3310  N   ASP A 453      17.749  -6.019  42.845  1.00 61.74      A
ATOM   3311  CA  ASP A 453      18.706  -5.119  43.467  1.00 61.74      A
ATOM   3312  CB  ASP A 453      18.484  -5.081  44.981  1.00 86.73      A
ATOM   3313  CG  ASP A 453      17.188  -4.384  45.356  1.00 86.73      A
ATOM   3314  OD1 ASP A 453      16.888  -4.279  46.566  1.00 86.73      A
ATOM   3315  OD2 ASP A 453      16.469  -3.939  44.435  1.00 86.73      A
ATOM   3316  C   ASP A 453      20.133  -5.528  43.144  1.00 61.74      A
ATOM   3317  O   ASP A 453      21.013  -4.683  43.009  1.00 61.74      A
ATOM   3318  N   LYS A 454      20.350  -6.828  42.993  1.00 52.02      A
ATOM   3319  CA  LYS A 454      21.676  -7.360  42.685  1.00 52.02      A
ATOM   3320  CB  LYS A 454      21.673  -8.887  42.818  1.00126.78      A
ATOM   3321  CG  LYS A 454      20.631  -9.439  43.785  1.00126.78      A
ATOM   3322  CD  LYS A 454      19.233  -9.396  43.175  1.00126.78      A
ATOM   3323  CE  LYS A 454      18.173  -9.896  44.141  1.00126.78      A
ATOM   3324  NZ  LYS A 454      18.061  -9.024  45.340  1.00126.78      A
ATOM   3325  C   LYS A 454      22.109  -6.975  41.266  1.00 52.02      A
ATOM   3326  O   LYS A 454      23.288  -6.717  41.009  1.00 52.02      A
ATOM   3327  N   GLY A 455      21.154  -6.954  40.342  1.00 46.36      A
ATOM   3328  CA  GLY A 455      21.477  -6.599  38.970  1.00 46.36      A
ATOM   3329  C   GLY A 455      21.888  -5.138  38.895  1.00 46.36      A
ATOM   3330  O   GLY A 455      22.899  -4.788  38.277  1.00 46.36      A
ATOM   3331  N   ILE A 456      21.098  -4.290  39.544  1.00 53.41      A
ATOM   3332  CA  ILE A 456      21.365  -2.867  39.560  1.00 53.41      A
ATOM   3333  CB  ILE A 456      20.267  -2.119  40.333  1.00 42.96      A
ATOM   3334  CG2 ILE A 456      20.658  -0.643  40.515  1.00 42.96      A
ATOM   3335  CG1 ILE A 456      18.945  -2.253  39.562  1.00 42.96      A
ATOM   3336  CD1 ILE A 456      17.736  -1.670  40.260  1.00 42.96      A
ATOM   3337  C   ILE A 456      22.735  -2.595  40.163  1.00 53.41      A
ATOM   3338  O   ILE A 456      23.520  -1.840  39.591  1.00 53.41      A
ATOM   3339  N   ILE A 457      23.035  -3.224  41.299  1.00 59.64      A
ATOM   3340  CA  ILE A 457      24.341  -3.041  41.929  1.00 59.64      A
ATOM   3341  CB  ILE A 457      24.500  -3.931  43.192  1.00 70.44      A
ATOM   3342  CG2 ILE A 457      25.931  -3.884  43.695  1.00 70.44      A
ATOM   3343  CG1 ILE A 457      23.568  -3.441  44.300  1.00 70.44      A
ATOM   3344  CD1 ILE A 457      23.591  -4.315  45.537  1.00 70.44      A
ATOM   3345  C   ILE A 457      25.456  -3.371  40.933  1.00 59.64      A
```

FIGURE 25 CON'T

```
ATOM   3346  O   ILE A 457      26.413  -2.616  40.805  1.00 59.64      A
ATOM   3347  N   GLU A 458      25.325  -4.490  40.223  1.00 44.35      A
ATOM   3348  CA  GLU A 458      26.329  -4.902  39.233  1.00 44.35      A
ATOM   3349  CB  GLU A 458      25.943  -6.244  38.604  1.00 77.66      A
ATOM   3350  CG  GLU A 458      26.894  -7.404  38.901  1.00 77.66      A
ATOM   3351  CD  GLU A 458      28.335  -7.136  38.476  1.00 77.66      A
ATOM   3352  OE1 GLU A 458      29.066  -6.476  39.240  1.00 77.66      A
ATOM   3353  OE2 GLU A 458      28.739  -7.577  37.378  1.00 77.66      A
ATOM   3354  C   GLU A 458      26.497  -3.854  38.122  1.00 44.35      A
ATOM   3355  O   GLU A 458      27.614  -3.598  37.672  1.00 44.35      A

ATOM   3356  N   VAL A 459      25.392  -3.256  37.677  1.00 40.06      A
ATOM   3357  CA  VAL A 459      25.453  -2.237  36.624  1.00 40.06      A
ATOM   3358  CB  VAL A 459      24.043  -1.675  36.268  1.00 38.40      A
ATOM   3359  CG1 VAL A 459      24.173  -0.545  35.234  1.00 38.40      A
ATOM   3360  CG2 VAL A 459      23.162  -2.786  35.713  1.00 38.40      A
ATOM   3361  C   VAL A 459      26.326  -1.071  37.077  1.00 40.06      A
ATOM   3362  O   VAL A 459      27.297  -0.708  36.409  1.00 40.06      A
ATOM   3363  N   VAL A 460      25.949  -0.492  38.212  1.00 44.57      A
ATOM   3364  CA  VAL A 460      26.648   0.633  38.812  1.00 44.57      A
ATOM   3365  CB  VAL A 460      26.020   0.959  40.184  1.00 43.98      A
ATOM   3366  CG1 VAL A 460      26.690   2.184  40.816  1.00 43.98      A
ATOM   3367  CG2 VAL A 460      24.542   1.205  40.004  1.00 43.98      A
ATOM   3368  C   VAL A 460      28.147   0.349  38.964  1.00 44.57      A
ATOM   3369  O   VAL A 460      28.976   1.173  38.583  1.00 44.57      A
ATOM   3370  N   GLU A 461      28.488  -0.825  39.491  1.00 47.44      A
ATOM   3371  CA  GLU A 461      29.889  -1.209  39.672  1.00 47.44      A
ATOM   3372  CB  GLU A 461      29.988  -2.578  40.349  1.00 98.43      A
ATOM   3373  CG  GLU A 461      29.828  -2.551  41.857  1.00 98.43      A
ATOM   3374  CD  GLU A 461      29.867  -3.941  42.467  1.00 98.43      A
ATOM   3375  OE1 GLU A 461      30.758  -4.732  42.090  1.00 98.43      A
ATOM   3376  OE2 GLU A 461      29.013  -4.242  43.326  1.00 98.43      A
ATOM   3377  C   GLU A 461      30.631  -1.250  38.343  1.00 47.44      A
ATOM   3378  O   GLU A 461      31.739  -0.721  38.223  1.00 47.44      A
ATOM   3379  N   GLN A 462      30.025  -1.884  37.345  1.00 44.62      A
ATOM   3380  CA  GLN A 462      30.647  -1.968  36.025  1.00 44.62      A
ATOM   3381  CB  GLN A 462      29.803  -2.824  35.069  1.00 80.21      A
ATOM   3382  CG  GLN A 462      29.788  -4.317  35.380  1.00 80.21      A
ATOM   3383  CD  GLN A 462      29.154  -5.144  34.262  1.00 80.21      A
ATOM   3384  OE1 GLN A 462      29.584  -5.085  33.106  1.00 80.21      A
ATOM   3385  NE2 GLN A 462      28.133  -5.926  34.605  1.00 80.21      A
ATOM   3386  C   GLN A 462      30.824  -0.572  35.430  1.00 44.62      A
ATOM   3387  O   GLN A 462      31.884  -0.252  34.885  1.00 44.62      A
ATOM   3388  N   VAL A 463      29.795   0.267  35.537  1.00 47.32      A
ATOM   3389  CA  VAL A 463      29.911   1.611  34.985  1.00 47.32      A
ATOM   3390  CB  VAL A 463      28.556   2.380  34.980  1.00 38.58      A
ATOM   3391  CG1 VAL A 463      28.775   3.792  34.482  1.00 38.58      A
ATOM   3392  CG2 VAL A 463      27.546   1.677  34.090  1.00 38.58      A
ATOM   3393  C   VAL A 463      30.941   2.450  35.752  1.00 47.32      A
ATOM   3394  O   VAL A 463      31.741   3.147  35.134  1.00 47.32      A
ATOM   3395  N   SER A 464      30.921   2.386  37.085  1.00 48.80      A
ATOM   3396  CA  SER A 464      31.866   3.171  37.883  1.00 48.80      A
ATOM   3397  CB  SER A 464      31.666   2.923  39.374  1.00 71.18      A
ATOM   3398  OG  SER A 464      32.154   1.651  39.735  1.00 71.18      A
ATOM   3399  C   SER A 464      33.288   2.810  37.495  1.00 48.80      A
ATOM   3400  O   SER A 464      34.163   3.674  37.415  1.00 48.80      A
ATOM   3401  N   SER A 465      33.508   1.526  37.236  1.00 54.68      A
```

FIGURE 25 CON'T

```
ATOM   3402  CA  SER A 465      34.822   1.045  36.838  1.00 54.68      A
ATOM   3403  CB  SER A 465      34.791  -0.477  36.685  1.00 66.14      A
ATOM   3404  OG  SER A 465      35.994  -0.943  36.107  1.00 66.14      A
ATOM   3405  C   SER A 465      35.313   1.682  35.533  1.00 54.68      A
ATOM   3406  O   SER A 465      36.501   1.976  35.388  1.00 54.68      A
ATOM   3407  N   PHE A 466      34.405   1.884  34.582  1.00 44.49      A
ATOM   3408  CA  PHE A 466      34.764   2.492  33.294  1.00 44.49      A
ATOM   3409  CB  PHE A 466      33.807   2.040  32.187  1.00 58.64      A
ATOM   3410  CG  PHE A 466      34.007   0.631  31.749  1.00 58.64      A
ATOM   3411  CD1 PHE A 466      33.524  -0.425  32.515  1.00 58.64      A
ATOM   3412  CD2 PHE A 466      34.694   0.353  30.570  1.00 58.64      A
ATOM   3413  CE1 PHE A 466      33.723  -1.750  32.116  1.00 58.64      A
ATOM   3414  CE2 PHE A 466      34.899  -0.960  30.161  1.00 58.64      A
ATOM   3415  CZ  PHE A 466      34.411  -2.018  30.939  1.00 58.64      A
ATOM   3416  C   PHE A 466      34.745   4.015  33.316  1.00 44.49      A
ATOM   3417  O   PHE A 466      35.256   4.647  32.394  1.00 44.49      A
ATOM   3418  N   MSE A 467      34.152   4.597  34.355  1.00 42.37      A
ATOM   3419  CA  MSE A 467      34.033   6.053  34.468  1.00 42.37      A
ATOM   3420  CB  MSE A 467      32.664   6.437  35.042  1.00 42.50      A
ATOM   3421  CG  MSE A 467      31.524   6.466  34.044  1.00 42.50      A
ATOM   3422  SE  MSE A 467      31.884   7.652  32.579  1.00 42.50      A
ATOM   3423  CE  MSE A 467      31.829   9.324  33.526  1.00 42.50      A
ATOM   3424  C   MSE A 467      35.092   6.751  35.321  1.00 42.37      A
ATOM   3425  O   MSE A 467      35.136   7.978  35.352  1.00 42.37      A
ATOM   3426  N   LYS A 468      35.913   5.993  36.036  1.00 42.40      A
ATOM   3427  CA  LYS A 468      36.927   6.622  36.877  1.00 42.40      A
ATOM   3428  CB  LYS A 468      37.738   5.572  37.654  1.00 74.83      A
ATOM   3429  CG  LYS A 468      38.409   4.495  36.813  1.00 74.83      A
ATOM   3430  CD  LYS A 468      39.342   3.654  37.689  1.00 74.83      A
ATOM   3431  CE  LYS A 468      39.923   2.453  36.955  1.00 74.83      A
ATOM   3432  NZ  LYS A 468      38.920   1.365  36.764  1.00 74.83      A
ATOM   3433  C   LYS A 468      37.850   7.492  36.037  1.00 42.40      A
ATOM   3434  O   LYS A 468      38.295   7.088  34.962  1.00 42.40      A
ATOM   3435  N   GLY A 469      38.113   8.700  36.521  1.00 46.88      A
ATOM   3436  CA  GLY A 469      38.981   9.600  35.785  1.00 46.88      A
ATOM   3437  C   GLY A 469      38.279  10.279  34.625  1.00 46.88      A
ATOM   3438  O   GLY A 469      38.910  10.997  33.844  1.00 46.88      A
ATOM   3439  N   LYS A 470      36.970  10.056  34.512  1.00 47.53      A
ATOM   3440  CA  LYS A 470      36.179  10.650  33.440  1.00 47.53      A
ATOM   3441  CB  LYS A 470      35.383   9.574  32.704  1.00 66.54      A
ATOM   3442  CG  LYS A 470      36.119   8.980  31.516  1.00 66.54      A
ATOM   3443  CD  LYS A 470      37.494   8.481  31.894  1.00 66.54      A
ATOM   3444  CE  LYS A 470      38.190   7.822  30.710  1.00 66.54      A
ATOM   3445  NZ  LYS A 470      37.472   6.586  30.287  1.00 66.54      A
ATOM   3446  C   LYS A 470      35.243  11.716  33.962  1.00 47.53      A
ATOM   3447  O   LYS A 470      34.720  11.615  35.072  1.00 47.53      A
ATOM   3448  N   GLU A 471      35.030  12.735  33.141  1.00 48.09      A
ATOM   3449  CA  GLU A 471      34.180  13.858  33.511  1.00 48.09      A
ATOM   3450  CB  GLU A 471      34.674  15.128  32.813  1.00 81.57      A
ATOM   3451  CG  GLU A 471      34.887  16.305  33.748  1.00 81.57      A
ATOM   3452  CD  GLU A 471      35.385  17.537  33.022  1.00 81.57      A
ATOM   3453  OE1 GLU A 471      36.456  17.460  32.382  1.00 81.57      A
ATOM   3454  OE2 GLU A 471      34.706  18.582  33.092  1.00 81.57      A
ATOM   3455  C   GLU A 471      32.705  13.655  33.186  1.00 48.09      A
ATOM   3456  O   GLU A 471      31.835  14.164  33.895  1.00 48.09      A
ATOM   3457  N   LEU A 472      32.413  12.898  32.131  1.00 39.18      A
ATOM   3458  CA  LEU A 472      31.020  12.718  31.748  1.00 39.18      A
```

FIGURE 25 CON'T

ATOM	3459	CB	LEU	A	472	30.575	13.901	30.880	1.00	52.26	A
ATOM	3460	CG	LEU	A	472	29.125	14.391	30.824	1.00	52.26	A
ATOM	3461	CD1	LEU	A	472	28.958	15.236	29.562	1.00	52.26	A
ATOM	3462	CD2	LEU	A	472	28.152	13.237	30.810	1.00	52.26	A
ATOM	3463	C	LEU	A	472	30.811	11.447	30.973	1.00	39.18	A
ATOM	3464	O	LEU	A	472	31.648	11.058	30.158	1.00	39.18	A
ATOM	3465	N	GLY	A	473	29.673	10.813	31.225	1.00	40.26	A
ATOM	3466	CA	GLY	A	473	29.327	9.598	30.518	1.00	40.26	A
ATOM	3467	C	GLY	A	473	27.844	9.640	30.185	1.00	40.26	A
ATOM	3468	O	GLY	A	473	27.103	10.446	30.750	1.00	40.26	A
ATOM	3469	N	LEU	A	474	27.416	8.775	29.273	1.00	42.74	A
ATOM	3470	CA	LEU	A	474	26.017	8.697	28.872	1.00	42.74	A
ATOM	3471	CB	LEU	A	474	25.831	9.263	27.458	1.00	61.12	A
ATOM	3472	CG	LEU	A	474	25.916	10.784	27.322	1.00	61.12	A
ATOM	3473	CD1	LEU	A	474	25.957	11.169	25.855	1.00	61.12	A
ATOM	3474	CD2	LEU	A	474	24.718	11.418	28.004	1.00	61.12	A
ATOM	3475	C	LEU	A	474	25.566	7.244	28.902	1.00	42.74	A
ATOM	3476	O	LEU	A	474	26.281	6.349	28.442	1.00	42.74	A
ATOM	3477	N	ALA	A	475	24.388	7.008	29.458	1.00	39.49	A
ATOM	3478	CA	ALA	A	475	23.863	5.657	29.523	1.00	39.49	A
ATOM	3479	CB	ALA	A	475	23.805	5.168	30.976	1.00	27.45	A
ATOM	3480	C	ALA	A	475	22.475	5.601	28.895	1.00	39.49	A
ATOM	3481	O	ALA	A	475	21.597	6.398	29.229	1.00	39.49	A
ATOM	3482	N	PHE	A	476	22.305	4.657	27.975	1.00	36.70	A
ATOM	3483	CA	PHE	A	476	21.040	4.435	27.289	1.00	36.70	A
ATOM	3484	CB	PHE	A	476	21.268	4.420	25.776	1.00	42.67	A
ATOM	3485	CG	PHE	A	476	21.771	5.732	25.254	1.00	42.67	A
ATOM	3486	CD1	PHE	A	476	20.898	6.789	25.044	1.00	42.67	A
ATOM	3487	CD2	PHE	A	476	23.132	5.951	25.094	1.00	42.67	A
ATOM	3488	CE1	PHE	A	476	21.370	8.051	24.690	1.00	42.67	A
ATOM	3489	CE2	PHE	A	476	23.620	7.213	24.740	1.00	42.67	A
ATOM	3490	CZ	PHE	A	476	22.735	8.267	24.539	1.00	42.67	A
ATOM	3491	C	PHE	A	476	20.562	3.103	27.823	1.00	36.70	A
ATOM	3492	O	PHE	A	476	21.233	2.073	27.674	1.00	36.70	A
ATOM	3493	N	ILE	A	477	19.396	3.155	28.460	1.00	35.04	A
ATOM	3494	CA	ILE	A	477	18.801	2.015	29.122	1.00	35.04	A
ATOM	3495	CB	ILE	A	477	18.587	2.373	30.607	1.00	32.38	A
ATOM	3496	CG2	ILE	A	477	18.258	1.118	31.410	1.00	32.38	A
ATOM	3497	CG1	ILE	A	477	19.854	3.050	31.150	1.00	32.38	A
ATOM	3498	CD1	ILE	A	477	19.719	3.619	32.567	1.00	32.38	A
ATOM	3499	C	ILE	A	477	17.480	1.494	28.554	1.00	35.04	A
ATOM	3500	O	ILE	A	477	16.520	2.241	28.385	1.00	35.04	A
ATOM	3501	N	ALA	A	478	17.444	0.198	28.277	1.00	43.08	A
ATOM	3502	CA	ALA	A	478	16.246	-0.453	27.769	1.00	43.08	A
ATOM	3503	CB	ALA	A	478	16.585	-1.317	26.549	1.00	35.21	A
ATOM	3504	C	ALA	A	478	15.786	-1.327	28.922	1.00	43.08	A
ATOM	3505	O	ALA	A	478	16.532	-2.199	29.366	1.00	43.08	A
ATOM	3506	N	ALA	A	479	14.569	-1.096	29.402	1.00	41.88	A
ATOM	3507	CA	ALA	A	479	14.026	-1.856	30.524	1.00	41.88	A
ATOM	3508	CB	ALA	A	479	14.095	-1.018	31.773	1.00	31.33	A
ATOM	3509	C	ALA	A	479	12.586	-2.314	30.324	1.00	41.88	A
ATOM	3510	O	ALA	A	479	11.834	-1.715	29.560	1.00	41.88	A
ATOM	3511	N	ARG	A	480	12.202	-3.363	31.043	1.00	51.72	A
ATOM	3512	CA	ARG	A	480	10.835	-3.865	30.976	1.00	51.72	A
ATOM	3513	CB	ARG	A	480	10.717	-5.184	31.737	1.00	64.52	A
ATOM	3514	CG	ARG	A	480	11.683	-6.237	31.248	1.00	64.52	A

FIGURE 25 CON'T

```
ATOM   3515  CD  ARG A 480      11.326  -7.615  31.746  1.00 64.52      A
ATOM   3516  NE  ARG A 480      11.570  -7.801  33.172  1.00 64.52      A
ATOM   3517  CZ  ARG A 480      12.774  -7.806  33.730  1.00 64.52      A
ATOM   3518  NH1 ARG A 480      13.846  -7.624  32.986  1.00 64.52      A
ATOM   3519  NH2 ARG A 480      12.910  -8.029  35.024  1.00 64.52      A
ATOM   3520  C   ARG A 480       9.943  -2.811  31.625  1.00 51.72      A
ATOM   3521  O   ARG A 480      10.426  -1.972  32.389  1.00 51.72      A
ATOM   3522  N   ASN A 481       8.651  -2.842  31.325  1.00 50.98      A
ATOM   3523  CA  ASN A 481       7.732  -1.867  31.907  1.00 50.98      A
ATOM   3524  CB  ASN A 481       6.393  -1.873  31.165  1.00 75.37      A
ATOM   3525  CG  ASN A 481       6.545  -1.619  29.679  1.00 75.37      A
ATOM   3526  OD1 ASN A 481       7.153  -0.634  29.259  1.00 75.37      A
ATOM   3527  ND2 ASN A 481       5.981  -2.512  28.870  1.00 75.37      A
ATOM   3528  C   ASN A 481       7.482  -2.164  33.386  1.00 50.98      A
ATOM   3529  O   ASN A 481       7.078  -1.281  34.143  1.00 50.98      A
ATOM   3530  N   LYS A 482       7.751  -3.406  33.779  1.00 55.90      A
ATOM   3531  CA  LYS A 482       7.535  -3.894  35.142  1.00 55.90      A
ATOM   3532  CB  LYS A 482       7.775  -5.405  35.193  1.00153.22      A
ATOM   3533  CG  LYS A 482       6.810  -6.238  34.371  1.00153.22      A
ATOM   3534  CD  LYS A 482       7.054  -7.720  34.608  1.00153.22      A
ATOM   3535  CE  LYS A 482       6.021  -8.578  33.901  1.00153.22      A
ATOM   3536  NZ  LYS A 482       6.200 -10.023  34.213  1.00153.22      A
ATOM   3537  C   LYS A 482       8.332  -3.256  36.275  1.00 55.90      A
ATOM   3538  O   LYS A 482       7.918  -3.332  37.434  1.00 55.90      A
ATOM   3539  N   LEU A 483       9.481  -2.661  35.967  1.00 55.02      A
ATOM   3540  CA  LEU A 483      10.291  -2.043  37.013  1.00 55.02      A
ATOM   3541  CB  LEU A 483      11.551  -1.398  36.431  1.00 65.69      A
ATOM   3542  CG  LEU A 483      12.749  -2.294  36.121  1.00 65.69      A
ATOM   3543  CD1 LEU A 483      12.423  -3.201  34.947  1.00 65.69      A
ATOM   3544  CD2 LEU A 483      13.961  -1.421  35.805  1.00 65.69      A
ATOM   3545  C   LEU A 483       9.509  -0.989  37.779  1.00 55.02      A
ATOM   3546  O   LEU A 483       8.807  -0.169  37.186  1.00 55.02      A
ATOM   3547  N   SER A 484       9.635  -1.019  39.101  1.00 57.55      A
ATOM   3548  CA  SER A 484       8.954  -0.052  39.950  1.00 57.55      A
ATOM   3549  CB  SER A 484       9.173  -0.407  41.419  1.00 65.93      A
ATOM   3550  OG  SER A 484      10.555  -0.417  41.727  1.00 65.93      A
ATOM   3551  C   SER A 484       9.543   1.324  39.663  1.00 57.55      A
ATOM   3552  O   SER A 484      10.613   1.422  39.060  1.00 57.55      A
ATOM   3553  N   SER A 485       8.851   2.382  40.078  1.00 68.39      A
ATOM   3554  CA  SER A 485       9.351   3.737  39.856  1.00 68.39      A
ATOM   3555  CB  SER A 485       8.346   4.778  40.350  1.00 92.91      A
ATOM   3556  OG  SER A 485       7.168   4.761  39.569  1.00 92.91      A
ATOM   3557  C   SER A 485      10.650   3.891  40.631  1.00 68.39      A
ATOM   3558  O   SER A 485      11.587   4.552  40.186  1.00 68.39      A
ATOM   3559  N   GLU A 486      10.687   3.253  41.793  1.00 63.66      A
ATOM   3560  CA  GLU A 486      11.837   3.291  42.682  1.00 63.66      A
ATOM   3561  CB  GLU A 486      11.517   2.491  43.946  1.00137.76      A
ATOM   3562  CG  GLU A 486      12.596   2.505  45.006  1.00137.76      A
ATOM   3563  CD  GLU A 486      12.133   1.850  46.291  1.00137.76      A
ATOM   3564  OE1 GLU A 486      11.719   0.672  46.243  1.00137.76      A
ATOM   3565  OE2 GLU A 486      12.180   2.514  47.347  1.00137.76      A
ATOM   3566  C   GLU A 486      13.102   2.753  42.023  1.00 63.66      A
ATOM   3567  O   GLU A 486      14.154   3.394  42.074  1.00 63.66      A
ATOM   3568  N   LYS A 487      13.002   1.578  41.407  1.00 56.40      A
ATOM   3569  CA  LYS A 487      14.156   0.969  40.751  1.00 56.40      A
ATOM   3570  CB  LYS A 487      13.819  -0.451  40.297  1.00 87.04      A
ATOM   3571  CG  LYS A 487      13.731  -1.417  41.465  1.00 87.04      A
```

FIGURE 25 CON'T

```
ATOM   3572  CD  LYS A 487      13.418  -2.834  41.032  1.00 87.04      A
ATOM   3573  CE  LYS A 487      13.405  -3.758  42.238  1.00 87.04      A
ATOM   3574  NZ  LYS A 487      12.976  -5.133  41.883  1.00 87.04      A
ATOM   3575  C   LYS A 487      14.679   1.800  39.584  1.00 56.40      A
ATOM   3576  O   LYS A 487      15.885   1.867  39.361  1.00 56.40      A
ATOM   3577  N   PHE A 488      13.777   2.432  38.842  1.00 49.04      A
ATOM   3578  CA  PHE A 488      14.195   3.272  37.736  1.00 49.04      A
ATOM   3579  CB  PHE A 488      12.982   3.769  36.947  1.00 62.57      A
ATOM   3580  CG  PHE A 488      12.550   2.843  35.842  1.00 62.57      A
ATOM   3581  CD1 PHE A 488      13.434   2.494  34.824  1.00 62.57      A
ATOM   3582  CD2 PHE A 488      11.249   2.341  35.801  1.00 62.57      A
ATOM   3583  CE1 PHE A 488      13.030   1.662  33.780  1.00 62.57      A
ATOM   3584  CE2 PHE A 488      10.834   1.506  34.760  1.00 62.57      A
ATOM   3585  CZ  PHE A 488      11.727   1.167  33.747  1.00 62.57      A
ATOM   3586  C   PHE A 488      14.964   4.463  38.326  1.00 49.04      A
ATOM   3587  O   PHE A 488      16.072   4.781  37.882  1.00 49.04      A
ATOM   3588  N   GLU A 489      14.370   5.101  39.337  1.00 55.24      A
ATOM   3589  CA  GLU A 489      14.980   6.248  40.001  1.00 55.24      A
ATOM   3590  CB  GLU A 489      14.055   6.774  41.107  1.00 68.39      A
ATOM   3591  CG  GLU A 489      14.609   7.969  41.883  1.00 68.39      A
ATOM   3592  CD  GLU A 489      14.405   9.298  41.169  1.00 68.39      A
ATOM   3593  OE1 GLU A 489      14.203   9.291  39.935  1.00 68.39      A
ATOM   3594  OE2 GLU A 489      14.458  10.351  41.845  1.00 68.39      A
ATOM   3595  C   GLU A 489      16.342   5.866  40.595  1.00 55.24      A
ATOM   3596  O   GLU A 489      17.320   6.597  40.440  1.00 55.24      A
ATOM   3597  N   GLU A 490      16.410   4.719  41.265  1.00 43.99      A
ATOM   3598  CA  GLU A 490      17.669   4.270  41.866  1.00 43.99      A
ATOM   3599  CB  GLU A 490      17.453   2.968  42.642  1.00158.89      A
ATOM   3600  CG  GLU A 490      16.534   3.124  43.846  1.00158.89      A
ATOM   3601  CD  GLU A 490      16.395   1.844  44.650  1.00158.89      A
ATOM   3602  OE1 GLU A 490      15.979   0.817  44.073  1.00158.89      A
ATOM   3603  OE2 GLU A 490      16.698   1.867  45.861  1.00158.89      A
ATOM   3604  C   GLU A 490      18.766   4.084  40.816  1.00 43.99      A
ATOM   3605  O   GLU A 490      19.922   4.490  41.015  1.00 43.99      A
ATOM   3606  N   ILE A 491      18.402   3.473  39.691  1.00 40.00      A
ATOM   3607  CA  ILE A 491      19.357   3.254  38.607  1.00 40.00      A
ATOM   3608  CB  ILE A 491      18.687   2.515  37.418  1.00 42.91      A
ATOM   3609  CG2 ILE A 491      19.604   2.542  36.188  1.00 42.91      A
ATOM   3610  CG1 ILE A 491      18.362   1.070  37.823  1.00 42.91      A
ATOM   3611  CD1 ILE A 491      17.546   0.328  36.790  1.00 42.91      A

ATOM   3612  C   ILE A 491      19.923   4.585  38.114  1.00 40.00      A
ATOM   3613  O   ILE A 491      21.137   4.754  38.016  1.00 40.00      A
ATOM   3614  N   LYS A 492      19.034   5.530  37.825  1.00 45.61      A
ATOM   3615  CA  LYS A 492      19.434   6.838  37.322  1.00 45.61      A
ATOM   3616  CB  LYS A 492      18.200   7.647  36.911  1.00 73.74      A
ATOM   3617  CG  LYS A 492      17.380   7.014  35.795  1.00 73.74      A
ATOM   3618  CD  LYS A 492      16.412   8.012  35.170  1.00 73.74      A
ATOM   3619  CE  LYS A 492      15.412   8.545  36.182  1.00 73.74      A
ATOM   3620  NZ  LYS A 492      14.528   9.595  35.592  1.00 73.74      A
ATOM   3621  C   LYS A 492      20.273   7.662  38.300  1.00 45.61      A
ATOM   3622  O   LYS A 492      21.271   8.277  37.902  1.00 45.61      A
ATOM   3623  N   ARG A 493      19.863   7.675  39.569  1.00 38.59      A
ATOM   3624  CA  ARG A 493      20.562   8.436  40.594  1.00 38.59      A
ATOM   3625  CB  ARG A 493      19.751   8.412  41.905  1.00 58.59      A
ATOM   3626  CG  ARG A 493      20.469   9.034  43.107  1.00 58.59      A
ATOM   3627  CD  ARG A 493      19.544   9.274  44.297  1.00 58.59      A
```

FIGURE 25 CON'T

```
ATOM   3628  NE  ARG A 493      18.748   8.099  44.628  1.00 58.59      A
ATOM   3629  CZ  ARG A 493      19.232   6.981  45.159  1.00 58.59      A
ATOM   3630  NH1 ARG A 493      20.528   6.876  45.441  1.00 58.59      A
ATOM   3631  NH2 ARG A 493      18.415   5.954  45.381  1.00 58.59      A
ATOM   3632  C   ARG A 493      21.982   7.899  40.818  1.00 38.59      A
ATOM   3633  O   ARG A 493      22.944   8.672  40.889  1.00 38.59      A
ATOM   3634  N   ARG A 494      22.109   6.580  40.910  1.00 44.47      A
ATOM   3635  CA  ARG A 494      23.413   5.946  41.125  1.00 44.47      A
ATOM   3636  CB  ARG A 494      23.241   4.450  41.398  1.00 70.57      A
ATOM   3637  CG  ARG A 494      22.684   4.145  42.775  1.00 70.57      A
ATOM   3638  CD  ARG A 494      22.649   2.651  43.029  1.00 70.57      A
ATOM   3639  NE  ARG A 494      22.421   2.341  44.435  1.00 70.57      A
ATOM   3640  CZ  ARG A 494      21.321   2.662  45.110  1.00 70.57      A
ATOM   3641  NH1 ARG A 494      20.327   3.313  44.513  1.00 70.57      A
ATOM   3642  NH2 ARG A 494      21.216   2.328  46.389  1.00 70.57      A
ATOM   3643  C   ARG A 494      24.359   6.146  39.943  1.00 44.47      A
ATOM   3644  O   ARG A 494      25.572   6.294  40.129  1.00 44.47      A
ATOM   3645  N   LEU A 495      23.820   6.142  38.726  1.00 32.24      A
ATOM   3646  CA  LEU A 495      24.685   6.358  37.578  1.00 32.24      A
ATOM   3647  CB  LEU A 495      23.971   6.042  36.266  1.00 37.98      A
ATOM   3648  CG  LEU A 495      23.668   4.549  36.102  1.00 37.98      A
ATOM   3649  CD1 LEU A 495      22.747   4.315  34.894  1.00 37.98      A
ATOM   3650  CD2 LEU A 495      24.977   3.784  35.968  1.00 37.98      A
ATOM   3651  C   LEU A 495      25.132   7.800  37.598  1.00 32.24      A
ATOM   3652  O   LEU A 495      26.296   8.098  37.290  1.00 32.24      A
ATOM   3653  N   PHE A 496      24.238   8.704  37.992  1.00 41.94      A
ATOM   3654  CA  PHE A 496      24.641  10.097  38.011  1.00 41.94      A
ATOM   3655  CB  PHE A 496      23.471  11.053  38.247  1.00 34.82      A
ATOM   3656  CG  PHE A 496      23.860  12.502  38.070  1.00 34.82      A
ATOM   3657  CD1 PHE A 496      24.164  13.001  36.806  1.00 34.82      A
ATOM   3658  CD2 PHE A 496      24.033  13.330  39.169  1.00 34.82      A
ATOM   3659  CE1 PHE A 496      24.646  14.303  36.641  1.00 34.82      A
ATOM   3660  CE2 PHE A 496      24.516  14.636  39.021  1.00 34.82      A
ATOM   3661  CZ  PHE A 496      24.825  15.124  37.752  1.00 34.82      A
ATOM   3662  C   PHE A 496      25.723  10.373  39.051  1.00 41.94      A
ATOM   3663  O   PHE A 496      26.532  11.277  38.860  1.00 41.94      A
ATOM   3664  N   ASN A 497      25.737   9.624  40.153  1.00 43.40      A
ATOM   3665  CA  ASN A 497      26.779   9.837  41.160  1.00 43.40      A
ATOM   3666  CB  ASN A 497      26.649   8.862  42.334  1.00 48.67      A
ATOM   3667  CG  ASN A 497      25.547   9.250  43.293  1.00 48.67      A
ATOM   3668  OD1 ASN A 497      25.153  10.415  43.361  1.00 48.67      A
ATOM   3669  ND2 ASN A 497      25.050   8.279  44.053  1.00 48.67      A
ATOM   3670  C   ASN A 497      28.117   9.617  40.476  1.00 43.40      A
ATOM   3671  O   ASN A 497      29.145  10.132  40.914  1.00 43.40      A
ATOM   3672  N   LEU A 498      28.083   8.864  39.380  1.00 44.31      A
ATOM   3673  CA  LEU A 498      29.283   8.562  38.610  1.00 44.31      A
ATOM   3674  CB  LEU A 498      29.213   7.125  38.102  1.00 39.12      A
ATOM   3675  CG  LEU A 498      28.996   6.073  39.187  1.00 39.12      A
ATOM   3676  CD1 LEU A 498      28.786   4.711  38.542  1.00 39.12      A
ATOM   3677  CD2 LEU A 498      30.208   6.052  40.119  1.00 39.12      A
ATOM   3678  C   LEU A 498      29.485   9.502  37.421  1.00 44.31      A
ATOM   3679  O   LEU A 498      30.307   9.230  36.547  1.00 44.31      A
ATOM   3680  N   ASN A 499      28.751  10.610  37.394  1.00 41.29      A
ATOM   3681  CA  ASN A 499      28.840  11.562  36.281  1.00 41.29      A
ATOM   3682  CB  ASN A 499      30.289  11.976  35.981  1.00 51.72      A
ATOM   3683  CG  ASN A 499      30.914  12.799  37.082  1.00 51.72      A
ATOM   3684  OD1 ASN A 499      30.276  13.670  37.672  1.00 51.72      A
```

FIGURE 25 CON'T

ATOM	3685	ND2	ASN	A	499	32.191	12.540	37.346	1.00	51.72	A
ATOM	3686	C	ASN	A	499	28.264	10.967	35.000	1.00	41.29	A
ATOM	3687	O	ASN	A	499	28.703	11.312	33.902	1.00	41.29	A
ATOM	3688	N	VAL	A	500	27.303	10.062	35.131	1.00	42.36	A
ATOM	3689	CA	VAL	A	500	26.696	9.463	33.952	1.00	42.36	A
ATOM	3690	CB	VAL	A	500	26.783	7.916	34.003	1.00	38.46	A
ATOM	3691	CG1	VAL	A	500	26.070	7.305	32.786	1.00	38.46	A
ATOM	3692	CG2	VAL	A	500	28.259	7.483	34.017	1.00	38.46	A
ATOM	3693	C	VAL	A	500	25.238	9.891	33.848	1.00	42.36	A
ATOM	3694	O	VAL	A	500	24.434	9.628	34.753	1.00	42.36	A
ATOM	3695	N	ILE	A	501	24.909	10.572	32.755	1.00	36.97	A
ATOM	3696	CA	ILE	A	501	23.545	11.027	32.521	1.00	36.97	A
ATOM	3697	CB	ILE	A	501	23.498	12.270	31.587	1.00	40.00	A
ATOM	3698	CG2	ILE	A	501	22.047	12.747	31.416	1.00	40.00	A
ATOM	3699	CG1	ILE	A	501	24.383	13.393	32.140	1.00	40.00	A
ATOM	3700	CD1	ILE	A	501	24.030	13.826	33.503	1.00	40.00	A
ATOM	3701	C	ILE	A	501	22.888	9.855	31.803	1.00	36.97	A
ATOM	3702	O	ILE	A	501	23.525	9.217	30.965	1.00	36.97	A
ATOM	3703	N	SER	A	502	21.632	9.563	32.113	1.00	35.35	A
ATOM	3704	CA	SER	A	502	20.978	8.435	31.463	1.00	35.35	A
ATOM	3705	CB	SER	A	502	20.817	7.293	32.465	1.00	45.93	A
ATOM	3706	OG	SER	A	502	20.206	7.765	33.644	1.00	45.93	A
ATOM	3707	C	SER	A	502	19.630	8.732	30.796	1.00	35.35	A
ATOM	3708	O	SER	A	502	18.951	9.706	31.115	1.00	35.35	A
ATOM	3709	N	GLN	A	503	19.257	7.866	29.862	1.00	37.71	A
ATOM	3710	CA	GLN	A	503	18.008	8.006	29.124	1.00	37.71	A
ATOM	3711	CB	GLN	A	503	18.284	8.537	27.709	1.00	48.11	A
ATOM	3712	CG	GLN	A	503	17.046	8.679	26.840	1.00	48.11	A
ATOM	3713	CD	GLN	A	503	16.065	9.680	27.410	1.00	48.11	A
ATOM	3714	OE1	GLN	A	503	16.450	10.786	27.792	1.00	48.11	A
ATOM	3715	NE2	GLN	A	503	14.790	9.302	27.469	1.00	48.11	A
ATOM	3716	C	GLN	A	503	17.381	6.616	29.042	1.00	37.71	A
ATOM	3717	O	GLN	A	503	17.978	5.680	28.494	1.00	37.71	A
ATOM	3718	N	VAL	A	504	16.182	6.493	29.587	1.00	44.85	A
ATOM	3719	CA	VAL	A	504	15.480	5.225	29.600	1.00	44.85	A
ATOM	3720	CB	VAL	A	504	14.784	4.983	30.960	1.00	45.98	A
ATOM	3721	CG1	VAL	A	504	14.143	3.604	30.968	1.00	45.98	A
ATOM	3722	CG2	VAL	A	504	15.777	5.126	32.099	1.00	45.98	A
ATOM	3723	C	VAL	A	504	14.400	5.124	28.536	1.00	44.85	A
ATOM	3724	O	VAL	A	504	13.630	6.056	28.332	1.00	44.85	A
ATOM	3725	N	VAL	A	505	14.360	3.983	27.861	1.00	43.58	A
ATOM	3726	CA	VAL	A	505	13.337	3.685	26.866	1.00	43.58	A
ATOM	3727	CB	VAL	A	505	13.942	3.523	25.458	1.00	38.53	A
ATOM	3728	CG1	VAL	A	505	12.844	3.259	24.454	1.00	38.53	A
ATOM	3729	CG2	VAL	A	505	14.695	4.777	25.068	1.00	38.53	A
ATOM	3730	C	VAL	A	505	12.761	2.349	27.355	1.00	43.58	A
ATOM	3731	O	VAL	A	505	13.493	1.363	27.490	1.00	43.58	A
ATOM	3732	N	ASN	A	506	11.468	2.318	27.664	1.00	46.42	A
ATOM	3733	CA	ASN	A	506	10.859	1.085	28.159	1.00	46.42	A
ATOM	3734	CB	ASN	A	506	9.706	1.386	29.129	1.00	59.81	A
ATOM	3735	CG	ASN	A	506	8.601	2.214	28.493	1.00	59.81	A
ATOM	3736	OD1	ASN	A	506	8.264	2.030	27.326	1.00	59.81	A
ATOM	3737	ND2	ASN	A	506	8.022	3.122	29.269	1.00	59.81	A
ATOM	3738	C	ASN	A	506	10.363	0.172	27.048	1.00	46.42	A
ATOM	3739	O	ASN	A	506	10.230	0.587	25.902	1.00	46.42	A
ATOM	3740	N	GLU	A	507	10.095	-1.077	27.404	1.00	50.99	A

FIGURE 25 CON'T

```
ATOM   3741  CA  GLU A 507       9.627  -2.074  26.453  1.00 50.99      A
ATOM   3742  CB  GLU A 507       9.361  -3.395  27.181  1.00 59.87      A
ATOM   3743  CG  GLU A 507       9.132  -4.572  26.245  1.00 59.87      A
ATOM   3744  CD  GLU A 507       9.013  -5.901  26.970  1.00 59.87      A
ATOM   3745  OE1 GLU A 507       9.278  -6.942  26.325  1.00 59.87      A
ATOM   3746  OE2 GLU A 507       8.648  -5.912  28.172  1.00 59.87      A
ATOM   3747  C   GLU A 507       8.376  -1.659  25.653  1.00 50.99      A
ATOM   3748  O   GLU A 507       8.222  -2.060  24.491  1.00 50.99      A
ATOM   3749  N   ASP A 508       7.491  -0.865  26.253  1.00 52.41      A
ATOM   3750  CA  ASP A 508       6.282  -0.443  25.544  1.00 52.41      A
ATOM   3751  CB  ASP A 508       5.348   0.355  26.457  1.00 74.58      A
ATOM   3752  CG  ASP A 508       4.045   0.739  25.760  1.00 74.58      A
ATOM   3753  OD1 ASP A 508       3.995   1.799  25.097  1.00 74.58      A
ATOM   3754  OD2 ASP A 508       3.069  -0.035  25.860  1.00 74.58      A
ATOM   3755  C   ASP A 508       6.618   0.392  24.314  1.00 52.41      A
ATOM   3756  O   ASP A 508       6.090   0.154  23.225  1.00 52.41      A
ATOM   3757  N   THR A 509       7.494   1.370  24.491  1.00 49.23      A
ATOM   3758  CA  THR A 509       7.898   2.218  23.390  1.00 49.23      A
ATOM   3759  CB  THR A 509       8.894   3.294  23.860  1.00 43.42      A
ATOM   3760  OG1 THR A 509       8.289   4.091  24.884  1.00 43.42      A
ATOM   3761  CG2 THR A 509       9.296   4.171  22.703  1.00 43.42      A
ATOM   3762  C   THR A 509       8.571   1.383  22.304  1.00 49.23      A
ATOM   3763  O   THR A 509       8.295   1.552  21.121  1.00 49.23      A
ATOM   3764  N   LEU A 510       9.448   0.476  22.719  1.00 56.19      A
ATOM   3765  CA  LEU A 510      10.172  -0.370  21.787  1.00 56.19      A
ATOM   3766  CB  LEU A 510      11.199  -1.220  22.539  1.00 52.24      A
ATOM   3767  CG  LEU A 510      12.326  -0.427  23.220  1.00 52.24      A
ATOM   3768  CD1 LEU A 510      13.142  -1.331  24.147  1.00 52.24      A
ATOM   3769  CD2 LEU A 510      13.210   0.201  22.150  1.00 52.24      A
ATOM   3770  C   LEU A 510       9.268  -1.264  20.949  1.00 56.19      A
ATOM   3771  O   LEU A 510       9.521  -1.459  19.758  1.00 56.19      A
ATOM   3772  N   LYS A 511       8.209  -1.798  21.548  1.00 51.64      A
ATOM   3773  CA  LYS A 511       7.313  -2.670  20.795  1.00 51.64      A
ATOM   3774  CB  LYS A 511       6.653  -3.703  21.713  1.00 94.73      A
ATOM   3775  CG  LYS A 511       7.585  -4.810  22.183  1.00 94.73      A
ATOM   3776  CD  LYS A 511       6.809  -6.037  22.643  1.00 94.73      A
ATOM   3777  CE  LYS A 511       5.841  -5.711  23.769  1.00 94.73      A
ATOM   3778  NZ  LYS A 511       5.049  -6.906  24.160  1.00 94.73      A
ATOM   3779  C   LYS A 511       6.221  -1.965  19.997  1.00 51.64      A
ATOM   3780  O   LYS A 511       5.881  -2.411  18.901  1.00 51.64      A
ATOM   3781  N   ASN A 512       5.702  -0.854  20.516  1.00 57.85      A
ATOM   3782  CA  ASN A 512       4.600  -0.154  19.857  1.00 57.85      A
ATOM   3783  CB  ASN A 512       3.480   0.069  20.873  1.00 59.41      A
ATOM   3784  CG  ASN A 512       3.127  -1.192  21.621  1.00 59.41      A
ATOM   3785  OD1 ASN A 512       2.917  -2.241  21.017  1.00 59.41      A
ATOM   3786  ND2 ASN A 512       3.063  -1.100  22.943  1.00 59.41      A
ATOM   3787  C   ASN A 512       4.845   1.164  19.129  1.00 57.85      A
ATOM   3788  O   ASN A 512       3.890   1.782  18.665  1.00 57.85      A
ATOM   3789  N   LYS A 513       6.092   1.610  19.021  1.00 49.76      A
ATOM   3790  CA  LYS A 513       6.345   2.876  18.341  1.00 49.76      A
ATOM   3791  CB  LYS A 513       6.929   3.884  19.330  1.00 70.06      A
ATOM   3792  CG  LYS A 513       6.139   4.014  20.631  1.00 70.06      A
ATOM   3793  CD  LYS A 513       4.735   4.560  20.406  1.00 70.06      A
ATOM   3794  CE  LYS A 513       3.942   4.630  21.715  1.00 70.06      A
ATOM   3795  NZ  LYS A 513       4.545   5.562  22.721  1.00 70.06      A
ATOM   3796  C   LYS A 513       7.286   2.706  17.146  1.00 49.76      A
ATOM   3797  O   LYS A 513       8.074   3.597  16.826  1.00 49.76      A
```

FIGURE 25 CON'T

ATOM	3798	N	ARG	A	514	7.193	1.561	16.481	1.00	51.04	A
ATOM	3799	CA	ARG	A	514	8.050	1.279	15.335	1.00	51.04	A
ATOM	3800	CB	ARG	A	514	8.111	-0.233	15.098	1.00	95.38	A
ATOM	3801	CG	ARG	A	514	8.587	-1.013	16.315	1.00	95.38	A
ATOM	3802	CD	ARG	A	514	8.878	-2.471	15.996	1.00	95.38	A
ATOM	3803	NE	ARG	A	514	9.496	-3.151	17.133	1.00	95.38	A
ATOM	3804	CZ	ARG	A	514	10.039	-4.364	17.083	1.00	95.38	A
ATOM	3805	NH1	ARG	A	514	10.046	-5.044	15.945	1.00	95.38	A
ATOM	3806	NH2	ARG	A	514	10.582	-4.897	18.172	1.00	95.38	A
ATOM	3807	C	ARG	A	514	7.599	1.994	14.059	1.00	51.04	A
ATOM	3808	O	ARG	A	514	6.404	2.179	13.822	1.00	51.04	A
ATOM	3809	N	ASP	A	515	8.565	2.406	13.241	1.00	46.95	A
ATOM	3810	CA	ASP	A	515	8.252	3.090	11.987	1.00	46.95	A
ATOM	3811	CB	ASP	A	515	9.536	3.522	11.279	1.00	87.61	A
ATOM	3812	CG	ASP	A	515	9.282	4.543	10.191	1.00	87.61	A
ATOM	3813	OD1	ASP	A	515	8.817	5.657	10.519	1.00	87.61	A
ATOM	3814	OD2	ASP	A	515	9.541	4.233	9.012	1.00	87.61	A
ATOM	3815	C	ASP	A	515	7.458	2.128	11.091	1.00	46.95	A
ATOM	3816	O	ASP	A	515	7.786	0.944	10.992	1.00	46.95	A
ATOM	3817	N	LYS	A	516	6.413	2.639	10.451	1.00	56.69	A
ATOM	3818	CA	LYS	A	516	5.572	1.814	9.582	1.00	56.69	A
ATOM	3819	CB	LYS	A	516	4.366	2.619	9.087	1.00133.08		A
ATOM	3820	CG	LYS	A	516	3.336	2.925	10.162	1.00133.08		A
ATOM	3821	CD	LYS	A	516	2.118	3.617	9.568	1.00133.08		A
ATOM	3822	CE	LYS	A	516	1.061	3.889	10.625	1.00133.08		A
ATOM	3823	NZ	LYS	A	516	-0.126	4.578	10.045	1.00133.08		A
ATOM	3824	C	LYS	A	516	6.303	1.221	8.379	1.00	56.69	A
ATOM	3825	O	LYS	A	516	5.943	0.147	7.899	1.00	56.69	A
ATOM	3826	N	TYR	A	517	7.330	1.910	7.899	1.00	62.90	A
ATOM	3827	CA	TYR	A	517	8.072	1.428	6.742	1.00	62.90	A
ATOM	3828	CB	TYR	A	517	8.406	2.610	5.824	1.00	60.86	A
ATOM	3829	CG	TYR	A	517	7.175	3.178	5.154	1.00	60.86	A
ATOM	3830	CD1	TYR	A	517	6.535	2.478	4.135	1.00	60.86	A
ATOM	3831	CE1	TYR	A	517	5.360	2.957	3.556	1.00	60.86	A
ATOM	3832	CD2	TYR	A	517	6.613	4.383	5.583	1.00	60.86	A
ATOM	3833	CE2	TYR	A	517	5.435	4.871	5.015	1.00	60.86	A
ATOM	3834	CZ	TYR	A	517	4.815	4.149	4.003	1.00	60.86	A
ATOM	3835	OH	TYR	A	517	3.644	4.601	3.450	1.00	60.86	A
ATOM	3836	C	TYR	A	517	9.333	0.634	7.077	1.00	62.90	A
ATOM	3837	O	TYR	A	517	10.028	0.157	6.179	1.00	62.90	A
ATOM	3838	N	ASP	A	518	9.618	0.478	8.366	1.00	51.19	A
ATOM	3839	CA	ASP	A	518	10.798	-0.268	8.798	1.00	51.19	A
ATOM	3840	CB	ASP	A	518	12.052	0.601	8.635	1.00	47.24	A
ATOM	3841	CG	ASP	A	518	13.313	-0.100	9.112	1.00	47.24	A
ATOM	3842	OD1	ASP	A	518	13.266	-1.324	9.357	1.00	47.24	A
ATOM	3843	OD2	ASP	A	518	14.353	0.571	9.237	1.00	47.24	A
ATOM	3844	C	ASP	A	518	10.619	-0.677	10.259	1.00	51.19	A
ATOM	3845	O	ASP	A	518	10.949	0.087	11.174	1.00	51.19	A
ATOM	3846	N	ARG	A	519	10.092	-1.877	10.476	1.00	59.86	A
ATOM	3847	CA	ARG	A	519	9.847	-2.346	11.831	1.00	59.86	A
ATOM	3848	CB	ARG	A	519	9.089	-3.673	11.817	1.00124.95		A
ATOM	3849	CG	ARG	A	519	9.832	-4.834	11.189	1.00124.95		A
ATOM	3850	CD	ARG	A	519	9.214	-6.135	11.662	1.00124.95		A
ATOM	3851	NE	ARG	A	519	7.756	-6.046	11.675	1.00124.95		A
ATOM	3852	CZ	ARG	A	519	6.957	-6.917	12.283	1.00124.95		A
ATOM	3853	NH1	ARG	A	519	7.472	-7.952	12.932	1.00124.95		A
ATOM	3854	NH2	ARG	A	519	5.641	-6.747	12.249	1.00124.95		A

FIGURE 25 CON'T

```
ATOM   3855  C   ARG A 519      11.096  -2.497  12.691  1.00 59.86      A
ATOM   3856  O   ARG A 519      10.992  -2.766  13.883  1.00 59.86      A
ATOM   3857  N   ASN A 520      12.273  -2.343  12.097  1.00 58.96      A
ATOM   3858  CA  ASN A 520      13.502  -2.461  12.873  1.00 58.96      A
ATOM   3859  CB  ASN A 520      14.560  -3.239  12.093  1.00 76.47      A
ATOM   3860  CG  ASN A 520      14.190  -4.695  11.924  1.00 76.47      A
ATOM   3861  OD1 ASN A 520      13.951  -5.401  12.903  1.00 76.47      A
ATOM   3862  ND2 ASN A 520      14.134  -5.153  10.678  1.00 76.47      A
ATOM   3863  C   ASN A 520      13.996  -1.063  13.195  1.00 58.96      A
ATOM   3864  O   ASN A 520      15.175  -0.841  13.470  1.00 58.96      A
ATOM   3865  N   ARG A 521      13.059  -0.127  13.172  1.00 50.69      A
ATOM   3866  CA  ARG A 521      13.358   1.263  13.436  1.00 50.69      A
ATOM   3867  CB  ARG A 521      13.494   2.010  12.109  1.00 75.22      A

ATOM   3868  CG  ARG A 521      13.944   3.443  12.235  1.00 75.22      A
ATOM   3869  CD  ARG A 521      13.681   4.193  10.950  1.00 75.22      A
ATOM   3870  NE  ARG A 521      14.171   3.460   9.790  1.00 75.22      A
ATOM   3871  CZ  ARG A 521      14.201   3.955   8.560  1.00 75.22      A
ATOM   3872  NH1 ARG A 521      13.769   5.189   8.335  1.00 75.22      A
ATOM   3873  NH2 ARG A 521      14.662   3.218   7.557  1.00 75.22      A
ATOM   3874  C   ARG A 521      12.232   1.888  14.265  1.00 50.69      A
ATOM   3875  O   ARG A 521      11.045   1.589  14.071  1.00 50.69      A
ATOM   3876  N   LEU A 522      12.616   2.765  15.181  1.00 49.36      A
ATOM   3877  CA  LEU A 522      11.652   3.438  16.028  1.00 49.36      A
ATOM   3878  CB  LEU A 522      12.378   4.039  17.232  1.00 57.92      A
ATOM   3879  CG  LEU A 522      11.813   3.832  18.638  1.00 57.92      A
ATOM   3880  CD1 LEU A 522      11.188   2.456  18.776  1.00 57.92      A
ATOM   3881  CD2 LEU A 522      12.942   4.029  19.650  1.00 57.92      A
ATOM   3882  C   LEU A 522      10.993   4.532  15.197  1.00 49.36      A
ATOM   3883  O   LEU A 522      11.555   4.983  14.190  1.00 49.36      A
ATOM   3884  N   ASP A 523       9.796   4.937  15.615  1.00 56.16      A
ATOM   3885  CA  ASP A 523       9.021   5.985  14.951  1.00 56.16      A
ATOM   3886  CB  ASP A 523       7.761   6.291  15.764  1.00 97.14      A
ATOM   3887  CG  ASP A 523       6.495   6.025  14.997  1.00 97.14      A
ATOM   3888  OD1 ASP A 523       6.320   6.639  13.925  1.00 97.14      A
ATOM   3889  OD2 ASP A 523       5.675   5.206  15.467  1.00 97.14      A
ATOM   3890  C   ASP A 523       9.828   7.271  14.834  1.00 56.16      A
ATOM   3891  O   ASP A 523      10.724   7.521  15.638  1.00 56.16      A
ATOM   3892  N   LEU A 524       9.487   8.099  13.849  1.00 51.60      A
ATOM   3893  CA  LEU A 524      10.181   9.365  13.650  1.00 51.60      A
ATOM   3894  CB  LEU A 524       9.813   9.968  12.290  1.00 64.33      A
ATOM   3895  CG  LEU A 524      10.572  11.234  11.873  1.00 64.33      A
ATOM   3896  CD1 LEU A 524      12.066  10.928  11.765  1.00 64.33      A
ATOM   3897  CD2 LEU A 524      10.046  11.735  10.535  1.00 64.33      A
ATOM   3898  C   LEU A 524       9.819  10.349  14.766  1.00 51.60      A
ATOM   3899  O   LEU A 524      10.649  11.144  15.200  1.00 51.60      A
ATOM   3900  N   PHE A 525       8.572  10.300  15.218  1.00 49.11      A
ATOM   3901  CA  PHE A 525       8.116  11.186  16.288  1.00 49.11      A
ATOM   3902  CB  PHE A 525       6.636  10.943  16.580  1.00 60.02      A
ATOM   3903  CG  PHE A 525       6.102  11.751  17.738  1.00 60.02      A
ATOM   3904  CD1 PHE A 525       6.015  13.139  17.657  1.00 60.02      A
ATOM   3905  CD2 PHE A 525       5.665  11.122  18.902  1.00 60.02      A
ATOM   3906  CE1 PHE A 525       5.496  13.886  18.718  1.00 60.02      A
ATOM   3907  CE2 PHE A 525       5.146  11.861  19.965  1.00 60.02      A
ATOM   3908  CZ  PHE A 525       5.060  13.243  19.873  1.00 60.02      A
ATOM   3909  C   PHE A 525       8.930  10.895  17.548  1.00 49.11      A
ATOM   3910  O   PHE A 525       9.519  11.786  18.148  1.00 49.11      A
```

FIGURE 25 CON'T

ATOM	3911	N	VAL	A	526	8.935	9.627	17.939	1.00	45.36	A
ATOM	3912	CA	VAL	A	526	9.656	9.164	19.110	1.00	45.36	A
ATOM	3913	CB	VAL	A	526	9.429	7.648	19.310	1.00	54.70	A
ATOM	3914	CG1	VAL	A	526	10.281	7.125	20.452	1.00	54.70	A
ATOM	3915	CG2	VAL	A	526	7.957	7.388	19.595	1.00	54.70	A
ATOM	3916	C	VAL	A	526	11.151	9.459	18.996	1.00	45.36	A
ATOM	3917	O	VAL	A	526	11.757	9.972	19.936	1.00	45.36	A
ATOM	3918	N	ARG	A	527	11.744	9.154	17.845	1.00	46.49	A
ATOM	3919	CA	ARG	A	527	13.168	9.406	17.665	1.00	46.49	A
ATOM	3920	CB	ARG	A	527	13.619	9.000	16.267	1.00	49.55	A
ATOM	3921	CG	ARG	A	527	13.832	7.501	16.119	1.00	49.55	A
ATOM	3922	CD	ARG	A	527	14.556	7.187	14.826	1.00	49.55	A
ATOM	3923	NE	ARG	A	527	15.108	5.837	14.829	1.00	49.55	A
ATOM	3924	CZ	ARG	A	527	15.989	5.399	13.938	1.00	49.55	A
ATOM	3925	NH1	ARG	A	527	16.406	6.210	12.972	1.00	49.55	A
ATOM	3926	NH2	ARG	A	527	16.471	4.162	14.024	1.00	49.55	A
ATOM	3927	C	ARG	A	527	13.537	10.862	17.933	1.00	46.49	A
ATOM	3928	O	ARG	A	527	14.530	11.137	18.616	1.00	46.49	A
ATOM	3929	N	HIS	A	528	12.748	11.792	17.404	1.00	44.86	A
ATOM	3930	CA	HIS	A	528	13.020	13.209	17.632	1.00	44.86	A
ATOM	3931	CB	HIS	A	528	12.011	14.100	16.897	1.00	54.69	A
ATOM	3932	CG	HIS	A	528	12.390	14.415	15.485	1.00	54.69	A
ATOM	3933	CD2	HIS	A	528	13.002	15.498	14.950	1.00	54.69	A
ATOM	3934	ND1	HIS	A	528	12.142	13.557	14.436	1.00	54.69	A
ATOM	3935	CE1	HIS	A	528	12.580	14.099	13.314	1.00	54.69	A
ATOM	3936	NE2	HIS	A	528	13.107	15.277	13.598	1.00	54.69	A
ATOM	3937	C	HIS	A	528	12.953	13.536	19.121	1.00	44.86	A
ATOM	3938	O	HIS	A	528	13.829	14.216	19.665	1.00	44.86	A
ATOM	3939	N	ASN	A	529	11.904	13.062	19.781	1.00	44.63	A
ATOM	3940	CA	ASN	A	529	11.744	13.348	21.199	1.00	44.63	A
ATOM	3941	CB	ASN	A	529	10.326	12.994	21.632	1.00	60.00	A
ATOM	3942	CG	ASN	A	529	9.300	13.998	21.102	1.00	60.00	A
ATOM	3943	OD1	ASN	A	529	9.293	15.169	21.505	1.00	60.00	A
ATOM	3944	ND2	ASN	A	529	8.445	13.551	20.184	1.00	60.00	A
ATOM	3945	C	ASN	A	529	12.811	12.686	22.079	1.00	44.63	A
ATOM	3946	O	ASN	A	529	13.228	13.266	23.074	1.00	44.63	A
ATOM	3947	N	LEU	A	530	13.273	11.498	21.708	1.00	40.73	A
ATOM	3948	CA	LEU	A	530	14.327	10.854	22.483	1.00	40.73	A
ATOM	3949	CB	LEU	A	530	14.671	9.473	21.920	1.00	47.00	A
ATOM	3950	CG	LEU	A	530	13.791	8.315	22.388	1.00	47.00	A
ATOM	3951	CD1	LEU	A	530	14.301	7.016	21.747	1.00	47.00	A
ATOM	3952	CD2	LEU	A	530	13.820	8.226	23.934	1.00	47.00	A
ATOM	3953	C	LEU	A	530	15.546	11.762	22.399	1.00	40.73	A
ATOM	3954	O	LEU	A	530	16.183	12.060	23.411	1.00	40.73	A
ATOM	3955	N	LEU	A	531	15.849	12.217	21.186	1.00	39.87	A
ATOM	3956	CA	LEU	A	531	16.974	13.111	20.971	1.00	39.87	A
ATOM	3957	CB	LEU	A	531	17.130	13.380	19.470	1.00	52.35	A
ATOM	3958	CG	LEU	A	531	18.335	14.144	18.922	1.00	52.35	A
ATOM	3959	CD1	LEU	A	531	19.639	13.683	19.562	1.00	52.35	A
ATOM	3960	CD2	LEU	A	531	18.382	13.909	17.419	1.00	52.35	A
ATOM	3961	C	LEU	A	531	16.790	14.418	21.754	1.00	39.87	A
ATOM	3962	O	LEU	A	531	17.754	14.931	22.333	1.00	39.87	A
ATOM	3963	N	PHE	A	532	15.563	14.954	21.789	1.00	39.21	A
ATOM	3964	CA	PHE	A	532	15.292	16.197	22.538	1.00	39.21	A
ATOM	3965	CB	PHE	A	532	13.840	16.666	22.367	1.00	45.18	A
ATOM	3966	CG	PHE	A	532	13.475	17.085	20.971	1.00	45.18	A
ATOM	3967	CD1	PHE	A	532	14.452	17.344	20.012	1.00	45.18	A

FIGURE 25 CON'T

```
ATOM   3968  CD2 PHE A 532      12.131  17.232  20.619  1.00 45.18      A
ATOM   3969  CE1 PHE A 532      14.100  17.741  18.717  1.00 45.18      A
ATOM   3970  CE2 PHE A 532      11.761  17.632  19.318  1.00 45.18      A
ATOM   3971  CZ  PHE A 532      12.746  17.885  18.369  1.00 45.18      A
ATOM   3972  C   PHE A 532      15.518  16.000  24.047  1.00 39.21      A
ATOM   3973  O   PHE A 532      16.051  16.876  24.729  1.00 39.21      A
ATOM   3974  N   GLN A 533      15.068  14.857  24.562  1.00 36.89      A
ATOM   3975  CA  GLN A 533      15.202  14.536  25.979  1.00 36.89      A
ATOM   3976  CB  GLN A 533      14.529  13.202  26.293  1.00 50.19      A
ATOM   3977  CG  GLN A 533      13.024  13.284  26.378  1.00 50.19      A
ATOM   3978  CD  GLN A 533      12.387  11.963  26.783  1.00 50.19      A
ATOM   3979  OE1 GLN A 533      12.761  11.356  27.798  1.00 50.19      A
ATOM   3980  NE2 GLN A 533      11.417  11.516  25.997  1.00 50.19      A
ATOM   3981  C   GLN A 533      16.665  14.473  26.405  1.00 36.89      A
ATOM   3982  O   GLN A 533      17.049  15.093  27.388  1.00 36.89      A
ATOM   3983  N   VAL A 534      17.471  13.732  25.651  1.00 41.68      A
ATOM   3984  CA  VAL A 534      18.895  13.601  25.961  1.00 41.68      A
ATOM   3985  CB  VAL A 534      19.610  12.666  24.950  1.00 53.57      A
ATOM   3986  CG1 VAL A 534      21.090  12.544  25.308  1.00 53.57      A
ATOM   3987  CG2 VAL A 534      18.954  11.292  24.953  1.00 53.57      A
ATOM   3988  C   VAL A 534      19.560  14.972  25.919  1.00 41.68      A
ATOM   3989  O   VAL A 534      20.243  15.367  26.854  1.00 41.68      A
ATOM   3990  N   LEU A 535      19.337  15.694  24.825  1.00 37.41      A
ATOM   3991  CA  LEU A 535      19.908  17.023  24.639  1.00 37.41      A
ATOM   3992  CB  LEU A 535      19.413  17.611  23.305  1.00 47.41      A
ATOM   3993  CG  LEU A 535      20.364  17.677  22.098  1.00 47.41      A
ATOM   3994  CD1 LEU A 535      21.395  16.577  22.139  1.00 47.41      A
ATOM   3995  CD2 LEU A 535      19.546  17.624  20.808  1.00 47.41      A

ATOM   3996  C   LEU A 535      19.575  17.964  25.802  1.00 37.41      A
ATOM   3997  O   LEU A 535      20.424  18.726  26.256  1.00 37.41      A
ATOM   3998  N   SER A 536      18.344  17.904  26.297  1.00 36.01      A
ATOM   3999  CA  SER A 536      17.962  18.779  27.402  1.00 36.01      A
ATOM   4000  CB  SER A 536      16.444  18.768  27.609  1.00 47.05      A
ATOM   4001  OG  SER A 536      16.018  17.553  28.181  1.00 47.05      A
ATOM   4002  C   SER A 536      18.658  18.378  28.699  1.00 36.01      A
ATOM   4003  O   SER A 536      18.914  19.229  29.559  1.00 36.01      A
ATOM   4004  N   LYS A 537      18.961  17.088  28.839  1.00 40.88      A
ATOM   4005  CA  LYS A 537      19.649  16.603  30.030  1.00 40.88      A
ATOM   4006  CB  LYS A 537      19.630  15.070  30.070  1.00 40.82      A
ATOM   4007  CG  LYS A 537      18.268  14.540  30.488  1.00 40.82      A
ATOM   4008  CD  LYS A 537      18.142  13.038  30.420  1.00 40.82      A
ATOM   4009  CE  LYS A 537      16.717  12.630  30.808  1.00 40.82      A
ATOM   4010  NZ  LYS A 537      16.435  11.186  30.576  1.00 40.82      A
ATOM   4011  C   LYS A 537      21.086  17.133  30.051  1.00 40.88      A
ATOM   4012  O   LYS A 537      21.703  17.227  31.108  1.00 40.88      A
ATOM   4013  N   LEU A 538      21.591  17.514  28.881  1.00 43.77      A
ATOM   4014  CA  LEU A 538      22.946  18.036  28.752  1.00 43.77      A
ATOM   4015  CB  LEU A 538      23.636  17.379  27.553  1.00 42.60      A
ATOM   4016  CG  LEU A 538      23.637  15.845  27.593  1.00 42.60      A
ATOM   4017  CD1 LEU A 538      24.172  15.273  26.283  1.00 42.60      A
ATOM   4018  CD2 LEU A 538      24.464  15.375  28.776  1.00 42.60      A
ATOM   4019  C   LEU A 538      22.958  19.560  28.585  1.00 43.77      A
ATOM   4020  O   LEU A 538      23.963  20.136  28.161  1.00 43.77      A
ATOM   4021  N   GLY A 539      21.837  20.200  28.920  1.00 36.99      A
ATOM   4022  CA  GLY A 539      21.729  21.649  28.814  1.00 36.99      A
ATOM   4023  C   GLY A 539      21.835  22.237  27.408  1.00 36.99      A
```

FIGURE 25 CON'T

ATOM	4024	O	GLY	A	539	22.090	23.431	27.260	1.00	36.99	A
ATOM	4025	N	VAL	A	540	21.634	21.429	26.375	1.00	46.64	A
ATOM	4026	CA	VAL	A	540	21.734	21.925	25.004	1.00	46.64	A
ATOM	4027	CB	VAL	A	540	21.999	20.759	24.022	1.00	44.91	A
ATOM	4028	CG1	VAL	A	540	22.014	21.267	22.583	1.00	44.91	A
ATOM	4029	CG2	VAL	A	540	23.326	20.097	24.353	1.00	44.91	A
ATOM	4030	C	VAL	A	540	20.490	22.695	24.537	1.00	46.64	A
ATOM	4031	O	VAL	A	540	19.358	22.224	24.697	1.00	46.64	A
ATOM	4032	N	LYS	A	541	20.705	23.891	23.990	1.00	45.20	A
ATOM	4033	CA	LYS	A	541	19.612	24.719	23.463	1.00	45.20	A
ATOM	4034	CB	LYS	A	541	19.990	26.202	23.512	1.00	50.66	A
ATOM	4035	CG	LYS	A	541	19.743	26.869	24.857	1.00	50.66	A
ATOM	4036	CD	LYS	A	541	20.490	26.179	25.992	1.00	50.66	A
ATOM	4037	CE	LYS	A	541	20.064	26.729	27.344	1.00	50.66	A
ATOM	4038	NZ	LYS	A	541	20.719	25.993	28.463	1.00	50.66	A
ATOM	4039	C	LYS	A	541	19.407	24.281	22.014	1.00	45.20	A
ATOM	4040	O	LYS	A	541	19.873	24.926	21.081	1.00	45.20	A
ATOM	4041	N	TYR	A	542	18.694	23.176	21.846	1.00	46.76	A
ATOM	4042	CA	TYR	A	542	18.451	22.576	20.546	1.00	46.76	A
ATOM	4043	CB	TYR	A	542	18.260	21.078	20.758	1.00	41.50	A
ATOM	4044	CG	TYR	A	542	17.064	20.777	21.627	1.00	41.50	A
ATOM	4045	CD1	TYR	A	542	15.802	20.558	21.059	1.00	41.50	A
ATOM	4046	CE1	TYR	A	542	14.680	20.330	21.857	1.00	41.50	A
ATOM	4047	CD2	TYR	A	542	17.176	20.760	23.023	1.00	41.50	A
ATOM	4048	CE2	TYR	A	542	16.058	20.534	23.837	1.00	41.50	A
ATOM	4049	CZ	TYR	A	542	14.816	20.318	23.246	1.00	41.50	A
ATOM	4050	OH	TYR	A	542	13.709	20.078	24.029	1.00	41.50	A
ATOM	4051	C	TYR	A	542	17.261	23.148	19.771	1.00	46.76	A
ATOM	4052	O	TYR	A	542	16.955	22.697	18.666	1.00	46.76	A
ATOM	4053	N	TYR	A	543	16.606	24.147	20.343	1.00	41.18	A
ATOM	4054	CA	TYR	A	543	15.436	24.749	19.728	1.00	41.18	A
ATOM	4055	CB	TYR	A	543	14.166	24.235	20.429	1.00	43.99	A
ATOM	4056	CG	TYR	A	543	14.054	24.688	21.878	1.00	43.99	A
ATOM	4057	CD1	TYR	A	543	13.424	25.889	22.211	1.00	43.99	A
ATOM	4058	CE1	TYR	A	543	13.402	26.358	23.538	1.00	43.99	A
ATOM	4059	CD2	TYR	A	543	14.655	23.951	22.909	1.00	43.99	A
ATOM	4060	CE2	TYR	A	543	14.639	24.408	24.233	1.00	43.99	A
ATOM	4061	CZ	TYR	A	543	14.018	25.612	24.541	1.00	43.99	A
ATOM	4062	OH	TYR	A	543	14.064	26.094	25.841	1.00	43.99	A
ATOM	4063	C	TYR	A	543	15.489	26.263	19.864	1.00	41.18	A
ATOM	4064	O	TYR	A	543	16.318	26.806	20.601	1.00	41.18	A
ATOM	4065	N	VAL	A	544	14.595	26.939	19.147	1.00	45.44	A
ATOM	4066	CA	VAL	A	544	14.493	28.388	19.217	1.00	45.44	A
ATOM	4067	CB	VAL	A	544	15.125	29.076	17.981	1.00	53.29	A
ATOM	4068	CG1	VAL	A	544	14.355	28.716	16.714	1.00	53.29	A
ATOM	4069	CG2	VAL	A	544	15.152	30.582	18.191	1.00	53.29	A
ATOM	4070	C	VAL	A	544	13.011	28.750	19.327	1.00	45.44	A
ATOM	4071	O	VAL	A	544	12.152	28.162	18.664	1.00	45.44	A
ATOM	4072	N	LEU	A	545	12.725	29.706	20.197	1.00	52.59	A
ATOM	4073	CA	LEU	A	545	11.373	30.162	20.441	1.00	52.59	A
ATOM	4074	CB	LEU	A	545	11.173	30.317	21.950	1.00	45.83	A
ATOM	4075	CG	LEU	A	545	9.881	30.950	22.447	1.00	45.83	A
ATOM	4076	CD1	LEU	A	545	8.682	30.142	21.962	1.00	45.83	A
ATOM	4077	CD2	LEU	A	545	9.921	31.021	23.965	1.00	45.83	A
ATOM	4078	C	LEU	A	545	11.104	31.488	19.726	1.00	52.59	A
ATOM	4079	O	LEU	A	545	11.763	32.495	19.996	1.00	52.59	A
ATOM	4080	N	ASP	A	546	10.141	31.475	18.805	1.00	58.10	A

FIGURE 25 CON'T

```
ATOM   4081  CA  ASP A 546       9.771  32.671  18.049  1.00 58.10      A
ATOM   4082  CB  ASP A 546       9.050  32.281  16.751  1.00102.17      A
ATOM   4083  CG  ASP A 546       8.575  33.489  15.952  1.00102.17      A
ATOM   4084  OD1 ASP A 546       9.405  34.369  15.642  1.00102.17      A
ATOM   4085  OD2 ASP A 546       7.370  33.554  15.627  1.00102.17      A
ATOM   4086  C   ASP A 546       8.849  33.480  18.941  1.00 58.10      A
ATOM   4087  O   ASP A 546       7.680  33.690  18.628  1.00 58.10      A
ATOM   4088  N   TYR A 547       9.395  33.941  20.058  1.00 54.64      A
ATOM   4089  CA  TYR A 547       8.615  34.687  21.028  1.00 54.64      A
ATOM   4090  CB  TYR A 547       7.643  33.722  21.702  1.00 57.57      A
ATOM   4091  CG  TYR A 547       6.670  34.341  22.672  1.00 57.57      A
ATOM   4092  CD1 TYR A 547       5.573  35.073  22.219  1.00 57.57      A
ATOM   4093  CE1 TYR A 547       4.635  35.591  23.112  1.00 57.57      A
ATOM   4094  CD2 TYR A 547       6.813  34.149  24.041  1.00 57.57      A
ATOM   4095  CE2 TYR A 547       5.886  34.661  24.941  1.00 57.57      A
ATOM   4096  CZ  TYR A 547       4.796  35.378  24.472  1.00 57.57      A
ATOM   4097  OH  TYR A 547       3.855  35.852  25.362  1.00 57.57      A
ATOM   4098  C   TYR A 547       9.561  35.279  22.063  1.00 54.64      A
ATOM   4099  O   TYR A 547      10.635  34.735  22.318  1.00 54.64      A
ATOM   4100  N   ARG A 548       9.179  36.405  22.646  1.00 53.73      A
ATOM   4101  CA  ARG A 548       9.997  37.023  23.675  1.00 53.73      A
ATOM   4102  CB  ARG A 548      10.686  38.288  23.162  1.00110.76      A
ATOM   4103  CG  ARG A 548      12.106  38.065  22.681  1.00110.76      A
ATOM   4104  CD  ARG A 548      12.849  39.386  22.556  1.00110.76      A
ATOM   4105  NE  ARG A 548      14.244  39.203  22.164  1.00110.76      A
ATOM   4106  CZ  ARG A 548      15.132  38.494  22.855  1.00110.76      A
ATOM   4107  NH1 ARG A 548      14.776  37.892  23.983  1.00110.76      A
ATOM   4108  NH2 ARG A 548      16.381  38.390  22.421  1.00110.76      A
ATOM   4109  C   ARG A 548       9.104  37.372  24.844  1.00 53.73      A
ATOM   4110  O   ARG A 548       8.063  38.004  24.660  1.00 53.73      A
ATOM   4111  N   PHE A 549       9.496  36.934  26.039  1.00 47.22      A
ATOM   4112  CA  PHE A 549       8.731  37.220  27.255  1.00 47.22      A
ATOM   4113  CB  PHE A 549       9.114  36.247  28.379  1.00 45.14      A
ATOM   4114  CG  PHE A 549       8.630  34.845  28.154  1.00 45.14      A
ATOM   4115  CD1 PHE A 549       7.358  34.462  28.564  1.00 45.14      A
ATOM   4116  CD2 PHE A 549       9.413  33.931  27.465  1.00 45.14      A
ATOM   4117  CE1 PHE A 549       6.871  33.183  28.281  1.00 45.14      A
ATOM   4118  CE2 PHE A 549       8.934  32.651  27.175  1.00 45.14      A
ATOM   4119  CZ  PHE A 549       7.656  32.281  27.585  1.00 45.14      A
ATOM   4120  C   PHE A 549       9.087  38.630  27.665  1.00 47.22      A
ATOM   4121  O   PHE A 549      10.247  39.023  27.570  1.00 47.22      A
ATOM   4122  N   ASN A 550       8.092  39.391  28.108  1.00 51.51      A
ATOM   4123  CA  ASN A 550       8.305  40.768  28.540  1.00 51.51      A

ATOM   4124  CB  ASN A 550       6.988  41.554  28.473  1.00 74.53      A
ATOM   4125  CG  ASN A 550       7.180  43.050  28.694  1.00 74.53      A
ATOM   4126  OD1 ASN A 550       8.011  43.684  28.046  1.00 74.53      A
ATOM   4127  ND2 ASN A 550       6.402  43.619  29.607  1.00 74.53      A
ATOM   4128  C   ASN A 550       8.849  40.769  29.965  1.00 51.51      A
ATOM   4129  O   ASN A 550       8.351  41.480  30.838  1.00 51.51      A
ATOM   4130  N   TYR A 551       9.873  39.953  30.193  1.00 56.02      A
ATOM   4131  CA  TYR A 551      10.503  39.846  31.509  1.00 56.02      A
ATOM   4132  CB  TYR A 551       9.937  38.659  32.295  1.00 48.15      A
ATOM   4133  CG  TYR A 551       8.465  38.743  32.614  1.00 48.15      A
ATOM   4134  CD1 TYR A 551       8.005  39.517  33.680  1.00 48.15      A
ATOM   4135  CE1 TYR A 551       6.653  39.598  33.972  1.00 48.15      A
ATOM   4136  CD2 TYR A 551       7.527  38.052  31.847  1.00 48.15      A
```

FIGURE 25 CON'T

```
ATOM   4137  CE2 TYR A 551       6.171  38.131  32.130  1.00 48.15      A
ATOM   4138  CZ  TYR A 551       5.740  38.905  33.187  1.00 48.15      A
ATOM   4139  OH  TYR A 551       4.394  39.020  33.443  1.00 48.15      A
ATOM   4140  C   TYR A 551      11.987  39.606  31.315  1.00 56.02      A
ATOM   4141  O   TYR A 551      12.418  39.160  30.251  1.00 56.02      A
ATOM   4142  N   ASP A 552      12.771  39.900  32.343  1.00 47.98      A
ATOM   4143  CA  ASP A 552      14.207  39.657  32.266  1.00 47.98      A
ATOM   4144  CB  ASP A 552      14.940  40.449  33.355  1.00 50.83      A
ATOM   4145  CG  ASP A 552      14.885  41.944  33.115  1.00 50.83      A
ATOM   4146  OD1 ASP A 552      15.518  42.405  32.153  1.00 50.83      A
ATOM   4147  OD2 ASP A 552      14.198  42.654  33.876  1.00 50.83      A
ATOM   4148  C   ASP A 552      14.409  38.160  32.475  1.00 47.98      A
ATOM   4149  O   ASP A 552      15.180  37.519  31.765  1.00 47.98      A
ATOM   4150  N   TYR A 553      13.688  37.608  33.446  1.00 44.86      A
ATOM   4151  CA  TYR A 553      13.776  36.184  33.756  1.00 44.86      A
ATOM   4152  CB  TYR A 553      14.819  35.948  34.854  1.00 50.87      A
ATOM   4153  CG  TYR A 553      16.205  36.400  34.482  1.00 50.87      A
ATOM   4154  CD1 TYR A 553      16.973  35.668  33.585  1.00 50.87      A
ATOM   4155  CE1 TYR A 553      18.230  36.111  33.186  1.00 50.87      A
ATOM   4156  CD2 TYR A 553      16.731  37.597  34.985  1.00 50.87      A
ATOM   4157  CE2 TYR A 553      17.990  38.053  34.590  1.00 50.87      A
ATOM   4158  CZ  TYR A 553      18.732  37.308  33.690  1.00 50.87      A
ATOM   4159  OH  TYR A 553      19.969  37.754  33.269  1.00 50.87      A
ATOM   4160  C   TYR A 553      12.424  35.668  34.245  1.00 44.86      A
ATOM   4161  O   TYR A 553      11.642  36.411  34.840  1.00 44.86      A
ATOM   4162  N   ILE A 554      12.134  34.403  33.964  1.00 41.31      A
ATOM   4163  CA  ILE A 554      10.898  33.812  34.458  1.00 41.31      A
ATOM   4164  CB  ILE A 554      10.088  33.092  33.356  1.00 44.64      A
ATOM   4165  CG2 ILE A 554       8.914  32.333  33.993  1.00 44.64      A
ATOM   4166  CG1 ILE A 554       9.547  34.111  32.343  1.00 44.64      A
ATOM   4167  CD1 ILE A 554      10.576  34.628  31.369  1.00 44.64      A
ATOM   4168  C   ILE A 554      11.421  32.801  35.463  1.00 41.31      A
ATOM   4169  O   ILE A 554      12.253  31.963  35.125  1.00 41.31      A
ATOM   4170  N   ILE A 555      10.962  32.883  36.703  1.00 39.73      A
ATOM   4171  CA  ILE A 555      11.471  31.959  37.706  1.00 39.73      A
ATOM   4172  CB  ILE A 555      12.273  32.730  38.786  1.00 41.36      A
ATOM   4173  CG2 ILE A 555      12.782  31.776  39.854  1.00 41.36      A
ATOM   4174  CG1 ILE A 555      13.449  33.467  38.121  1.00 41.36      A
ATOM   4175  CD1 ILE A 555      14.381  34.168  39.098  1.00 41.36      A
ATOM   4176  C   ILE A 555      10.433  31.068  38.395  1.00 39.73      A
ATOM   4177  O   ILE A 555       9.391  31.541  38.834  1.00 39.73      A
ATOM   4178  N   GLY A 556      10.734  29.768  38.456  1.00 38.06      A
ATOM   4179  CA  GLY A 556       9.861  28.830  39.132  1.00 38.06      A
ATOM   4180  C   GLY A 556      10.552  28.428  40.430  1.00 38.06      A
ATOM   4181  O   GLY A 556      11.771  28.169  40.449  1.00 38.06      A
ATOM   4182  N   ILE A 557       9.800  28.390  41.522  1.00 45.42      A
ATOM   4183  CA  ILE A 557      10.366  27.989  42.805  1.00 45.42      A
ATOM   4184  CB  ILE A 557      10.328  29.128  43.857  1.00 46.97      A
ATOM   4185  CG2 ILE A 557      11.055  30.371  43.340  1.00 46.97      A
ATOM   4186  CG1 ILE A 557       8.871  29.445  44.203  1.00 46.97      A
ATOM   4187  CD1 ILE A 557       8.670  29.999  45.604  1.00 46.97      A
ATOM   4188  C   ILE A 557       9.541  26.845  43.387  1.00 45.42      A
ATOM   4189  O   ILE A 557       8.384  26.643  43.009  1.00 45.42      A
ATOM   4190  N   ASP A 558      10.144  26.105  44.311  1.00 46.09      A
ATOM   4191  CA  ASP A 558       9.454  25.025  44.989  1.00 46.09      A
ATOM   4192  CB  ASP A 558       9.761  23.673  44.346  1.00 55.82      A
ATOM   4193  CG  ASP A 558       8.826  22.585  44.831  1.00 55.82      A
```

FIGURE 25 CON'T

```
ATOM   4194  OD1 ASP A 558       7.601  22.817  44.821  1.00 55.82      A
ATOM   4195  OD2 ASP A 558       9.298  21.503  45.218  1.00 55.82      A
ATOM   4196  C   ASP A 558       9.927  25.038  46.432  1.00 46.09      A
ATOM   4197  O   ASP A 558      11.130  25.077  46.705  1.00 46.09      A
ATOM   4198  N   VAL A 559       8.979  25.029  47.359  1.00 47.12      A
ATOM   4199  CA  VAL A 559       9.317  25.051  48.773  1.00 47.12      A
ATOM   4200  CB  VAL A 559       8.472  26.103  49.531  1.00 49.73      A
ATOM   4201  CG1 VAL A 559       8.932  26.197  50.984  1.00 49.73      A
ATOM   4202  CG2 VAL A 559       8.597  27.453  48.847  1.00 49.73      A
ATOM   4203  C   VAL A 559       9.086  23.682  49.394  1.00 47.12      A
ATOM   4204  O   VAL A 559       7.951  23.237  49.514  1.00 47.12      A
ATOM   4205  N   ALA A 560      10.172  23.019  49.785  1.00 57.97      A
ATOM   4206  CA  ALA A 560      10.089  21.692  50.390  1.00 57.97      A
ATOM   4207  CB  ALA A 560       9.980  20.627  49.302  1.00 68.19      A
ATOM   4208  C   ALA A 560      11.325  21.439  51.242  1.00 57.97      A
ATOM   4209  O   ALA A 560      12.361  21.016  50.733  1.00 57.97      A
ATOM   4210  N   PRO A 561      11.228  21.686  52.553  1.00 70.30      A
ATOM   4211  CD  PRO A 561      10.071  22.267  53.252  1.00 81.67      A
ATOM   4212  CA  PRO A 561      12.347  21.489  53.480  1.00 70.30      A
ATOM   4213  CB  PRO A 561      11.748  21.883  54.827  1.00 81.67      A
ATOM   4214  CG  PRO A 561      10.727  22.909  54.445  1.00 81.67      A
ATOM   4215  C   PRO A 561      12.937  20.078  53.508  1.00 70.30      A
ATOM   4216  O   PRO A 561      12.214  19.086  53.589  1.00 70.30      A
ATOM   4217  N   MSE A 562      14.262  20.011  53.450  1.00 71.51      A
ATOM   4218  CA  MSE A 562      14.990  18.749  53.486  1.00 71.51      A
ATOM   4219  CB  MSE A 562      15.122  18.184  52.078  1.00192.18      A
ATOM   4220  CG  MSE A 562      15.864  19.102  51.136  1.00192.18      A
ATOM   4221  SE  MSE A 562      15.628  18.577  49.315  1.00192.18      A
ATOM   4222  CE  MSE A 562      14.311  19.882  48.783  1.00192.18      A
ATOM   4223  C   MSE A 562      16.377  19.021  54.077  1.00 71.51      A
ATOM   4224  O   MSE A 562      16.821  20.171  54.130  1.00 71.51      A
ATOM   4225  N   LYS A 563      17.060  17.973  54.523  1.00 84.31      A
ATOM   4226  CA  LYS A 563      18.383  18.148  55.106  1.00 84.31      A
ATOM   4227  CB  LYS A 563      18.360  17.782  56.592  1.00 92.57      A
ATOM   4228  CG  LYS A 563      19.658  18.069  57.321  1.00 92.57      A
ATOM   4229  CD  LYS A 563      19.527  17.781  58.806  1.00 92.57      A
ATOM   4230  CE  LYS A 563      20.819  18.096  59.543  1.00 92.57      A
ATOM   4231  NZ  LYS A 563      20.672  17.920  61.015  1.00 92.57      A
ATOM   4232  C   LYS A 563      19.420  17.308  54.382  1.00 84.31      A
ATOM   4233  O   LYS A 563      19.221  16.115  54.158  1.00 84.31      A
ATOM   4234  N   ARG A 564      20.530  17.940  54.015  1.00 79.02      A
ATOM   4235  CA  ARG A 564      21.593  17.246  53.312  1.00 79.02      A
ATOM   4236  CB  ARG A 564      21.527  17.571  51.821  1.00 67.59      A
ATOM   4237  CG  ARG A 564      20.213  17.153  51.189  1.00 67.59      A
ATOM   4238  CD  ARG A 564      20.351  17.014  49.705  1.00 67.59      A
ATOM   4239  NE  ARG A 564      21.530  16.235  49.353  1.00 67.59      A
ATOM   4240  CZ  ARG A 564      21.728  15.677  48.164  1.00 67.59      A
ATOM   4241  NH1 ARG A 564      20.816  15.807  47.207  1.00 67.59      A
ATOM   4242  NH2 ARG A 564      22.839  14.996  47.929  1.00 67.59      A
ATOM   4243  C   ARG A 564      22.969  17.590  53.862  1.00 79.02      A
ATOM   4244  O   ARG A 564      23.174  18.672  54.419  1.00 79.02      A
ATOM   4245  N   SER A 565      23.899  16.652  53.706  1.00109.76      A
ATOM   4246  CA  SER A 565      25.269  16.815  54.177  1.00109.76      A
ATOM   4247  CB  SER A 565      26.199  15.892  53.386  1.00 81.52      A
ATOM   4248  OG  SER A 565      25.831  14.533  53.560  1.00 81.52      A
ATOM   4249  C   SER A 565      25.732  18.261  54.046  1.00109.76      A
ATOM   4250  O   SER A 565      26.018  18.733  52.945  1.00109.76      A
```

FIGURE 25 CON'T

ATOM	4251	N	GLU	A	566	25.803	18.958	55.179	1.00168.06 A
ATOM	4252	CA	GLU	A	566	26.215	20.357	55.199	1.00168.06 A
ATOM	4253	CB	GLU	A	566	27.688	20.486	54.794	1.00142.20 A
ATOM	4254	CG	GLU	A	566	28.361	21.807	55.179	1.00142.20 A
ATOM	4255	CD	GLU	A	566	27.672	23.035	54.602	1.00142.20 A
ATOM	4256	OE1	GLU	A	566	26.566	23.381	55.069	1.00142.20 A
ATOM	4257	OE2	GLU	A	566	28.238	23.656	53.677	1.00142.20 A
ATOM	4258	C	GLU	A	566	25.331	21.102	54.203	1.00168.06 A
ATOM	4259	O	GLU	A	566	25.805	21.577	53.170	1.00168.06 A
ATOM	4260	N	GLY	A	567	24.042	21.194	54.513	1.00123.79 A
ATOM	4261	CA	GLY	A	567	23.136	21.873	53.611	1.00123.79 A
ATOM	4262	C	GLY	A	567	21.833	22.364	54.206	1.00123.79 A
ATOM	4263	O	GLY	A	567	21.628	23.572	54.317	1.00123.79 A
ATOM	4264	N	TYR	A	568	20.952	21.442	54.593	1.00 77.07 A
ATOM	4265	CA	TYR	A	568	19.649	21.820	55.143	1.00 77.07 A
ATOM	4266	CB	TYR	A	568	19.824	22.493	56.508	1.00128.97 A
ATOM	4267	CG	TYR	A	568	18.536	22.699	57.276	1.00128.97 A
ATOM	4268	CD1	TYR	A	568	18.557	22.938	58.650	1.00128.97 A
ATOM	4269	CE1	TYR	A	568	17.379	23.148	59.362	1.00128.97 A
ATOM	4270	CD2	TYR	A	568	17.299	22.675	56.631	1.00128.97 A
ATOM	4271	CE2	TYR	A	568	16.115	22.885	57.332	1.00128.97 A
ATOM	4272	CZ	TYR	A	568	16.162	23.121	58.697	1.00128.97 A
ATOM	4273	OH	TYR	A	568	14.993	23.337	59.392	1.00128.97 A
ATOM	4274	C	TYR	A	568	19.027	22.783	54.123	1.00 77.07 A
ATOM	4275	O	TYR	A	568	19.068	24.002	54.283	1.00 77.07 A
ATOM	4276	N	ILE	A	569	18.454	22.210	53.070	1.00 62.58 A
ATOM	4277	CA	ILE	A	569	17.874	22.986	51.984	1.00 62.58 A
ATOM	4278	CB	ILE	A	569	18.214	22.331	50.642	1.00 78.12 A
ATOM	4279	CG2	ILE	A	569	17.748	23.211	49.491	1.00 78.12 A
ATOM	4280	CG1	ILE	A	569	19.727	22.110	50.571	1.00 78.12 A
ATOM	4281	CD1	ILE	A	569	20.195	21.387	49.332	1.00 78.12 A
ATOM	4282	C	ILE	A	569	16.375	23.197	52.086	1.00 62.58 A
ATOM	4283	O	ILE	A	569	15.614	22.269	52.353	1.00 62.58 A
ATOM	4284	N	GLY	A	570	15.958	24.436	51.852	1.00 48.55 A
ATOM	4285	CA	GLY	A	570	14.549	24.769	51.941	1.00 48.55 A
ATOM	4286	C	GLY	A	570	13.752	24.635	50.656	1.00 48.55 A
ATOM	4287	O	GLY	A	570	12.531	24.732	50.684	1.00 48.55 A
ATOM	4288	N	GLY	A	571	14.427	24.419	49.532	1.00 44.27 A
ATOM	4289	CA	GLY	A	571	13.704	24.286	48.280	1.00 44.27 A
ATOM	4290	C	GLY	A	571	14.565	24.498	47.062	1.00 44.27 A
ATOM	4291	O	GLY	A	571	15.780	24.288	47.094	1.00 44.27 A
ATOM	4292	N	SER	A	572	13.951	24.952	45.980	1.00 40.81 A
ATOM	4293	CA	SER	A	572	14.703	25.145	44.758	1.00 40.81 A
ATOM	4294	CB	SER	A	572	14.616	23.878	43.920	1.00 44.63 A
ATOM	4295	OG	SER	A	572	13.279	23.716	43.480	1.00 44.63 A
ATOM	4296	C	SER	A	572	14.169	26.302	43.935	1.00 40.81 A
ATOM	4297	O	SER	A	572	13.168	26.917	44.289	1.00 40.81 A
ATOM	4298	N	ALA	A	573	14.848	26.577	42.823	1.00 45.14 A
ATOM	4299	CA	ALA	A	573	14.443	27.638	41.908	1.00 45.14 A
ATOM	4300	CB	ALA	A	573	14.930	29.008	42.407	1.00 42.74 A
ATOM	4301	C	ALA	A	573	15.027	27.349	40.537	1.00 45.14 A
ATOM	4302	O	ALA	A	573	16.190	26.943	40.413	1.00 45.14 A
ATOM	4303	N	VAL	A	574	14.211	27.541	39.510	1.00 43.22 A
ATOM	4304	CA	VAL	A	574	14.645	27.319	38.144	1.00 43.22 A
ATOM	4305	CB	VAL	A	574	13.914	26.131	37.501	1.00 36.40 A
ATOM	4306	CG1	VAL	A	574	14.371	25.970	36.053	1.00 36.40 A

FIGURE 25 CON'T

```
ATOM   4307  CG2 VAL A 574      14.198  24.859  38.295  1.00 36.40      A
ATOM   4308  C   VAL A 574      14.385  28.586  37.336  1.00 43.22      A
ATOM   4309  O   VAL A 574      13.285  29.139  37.336  1.00 43.22      A
ATOM   4310  N   MSE A 575      15.413  29.022  36.628  1.00 37.32      A
ATOM   4311  CA  MSE A 575      15.354  30.247  35.860  1.00 37.32      A
ATOM   4312  CB  MSE A 575      16.475  31.169  36.363  1.00 58.88      A
ATOM   4313  CG  MSE A 575      16.679  32.475  35.609  1.00 58.88      A
ATOM   4314  SE  MSE A 575      18.345  33.372  36.183  1.00 58.88      A
ATOM   4315  CE  MSE A 575      19.467  32.802  34.741  1.00 58.88      A
ATOM   4316  C   MSE A 575      15.461  30.070  34.355  1.00 37.32      A
ATOM   4317  O   MSE A 575      16.314  29.335  33.862  1.00 37.32      A
ATOM   4318  N   PHE A 576      14.581  30.768  33.640  1.00 37.08      A
ATOM   4319  CA  PHE A 576      14.567  30.785  32.179  1.00 37.08      A
ATOM   4320  CB  PHE A 576      13.195  30.352  31.631  1.00 38.91      A
ATOM   4321  CG  PHE A 576      12.965  28.870  31.651  1.00 38.91      A
ATOM   4322  CD1 PHE A 576      12.744  28.179  30.466  1.00 38.91      A
ATOM   4323  CD2 PHE A 576      12.926  28.173  32.854  1.00 38.91      A
ATOM   4324  CE1 PHE A 576      12.482  26.818  30.472  1.00 38.91      A
ATOM   4325  CE2 PHE A 576      12.662  26.799  32.872  1.00 38.91      A
ATOM   4326  CZ  PHE A 576      12.438  26.124  31.685  1.00 38.91      A
ATOM   4327  C   PHE A 576      14.791  32.243  31.785  1.00 37.08      A
ATOM   4328  O   PHE A 576      14.442  33.139  32.548  1.00 37.08      A
ATOM   4329  N   ASP A 577      15.357  32.489  30.607  1.00 47.44      A
ATOM   4330  CA  ASP A 577      15.559  33.866  30.170  1.00 47.44      A
ATOM   4331  CB  ASP A 577      16.885  34.011  29.397  1.00 45.16      A
ATOM   4332  CG  ASP A 577      16.962  33.106  28.192  1.00 45.16      A
ATOM   4333  OD1 ASP A 577      15.896  32.724  27.661  1.00 45.16      A
ATOM   4334  OD2 ASP A 577      18.087  32.780  27.756  1.00 45.16      A
ATOM   4335  C   ASP A 577      14.357  34.264  29.296  1.00 47.44      A
ATOM   4336  O   ASP A 577      13.490  33.431  29.004  1.00 47.44      A
ATOM   4337  N   SER A 578      14.293  35.523  28.878  1.00 48.69      A
ATOM   4338  CA  SER A 578      13.160  35.992  28.071  1.00 48.69      A
ATOM   4339  CB  SER A 578      13.271  37.500  27.826  1.00 56.23      A
ATOM   4340  OG  SER A 578      14.368  37.803  26.983  1.00 56.23      A
ATOM   4341  C   SER A 578      13.046  35.270  26.735  1.00 48.69      A
ATOM   4342  O   SER A 578      12.042  35.392  26.029  1.00 48.69      A
ATOM   4343  N   GLN A 579      14.076  34.505  26.399  1.00 44.48      A
ATOM   4344  CA  GLN A 579      14.106  33.776  25.140  1.00 44.48      A
ATOM   4345  CB  GLN A 579      15.543  33.730  24.627  1.00 84.17      A
ATOM   4346  CG  GLN A 579      15.676  33.788  23.126  1.00 84.17      A
ATOM   4347  CD  GLN A 579      17.112  33.619  22.676  1.00 84.17      A
ATOM   4348  OE1 GLN A 579      18.022  34.253  23.215  1.00 84.17      A
ATOM   4349  NE2 GLN A 579      17.323  32.767  21.679  1.00 84.17      A
ATOM   4350  C   GLN A 579      13.557  32.345  25.275  1.00 44.48      A
ATOM   4351  O   GLN A 579      13.575  31.576  24.315  1.00 44.48      A
ATOM   4352  N   GLY A 580      13.078  31.983  26.460  1.00 38.30      A
ATOM   4353  CA  GLY A 580      12.540  30.645  26.632  1.00 38.30      A
ATOM   4354  C   GLY A 580      13.553  29.530  26.859  1.00 38.30      A
ATOM   4355  O   GLY A 580      13.243  28.347  26.639  1.00 38.30      A
ATOM   4356  N   TYR A 581      14.766  29.895  27.275  1.00 45.22      A
ATOM   4357  CA  TYR A 581      15.797  28.898  27.557  1.00 45.22      A
ATOM   4358  CB  TYR A 581      17.122  29.245  26.883  1.00 50.66      A
ATOM   4359  CG  TYR A 581      17.105  29.220  25.377  1.00 50.66      A
ATOM   4360  CD1 TYR A 581      16.611  28.118  24.682  1.00 50.66      A
ATOM   4361  CE1 TYR A 581      16.641  28.073  23.289  1.00 50.66      A
ATOM   4362  CD2 TYR A 581      17.626  30.288  24.642  1.00 50.66      A
ATOM   4363  CE2 TYR A 581      17.662  30.256  23.253  1.00 50.66      A
```

FIGURE 25 CON'T

ATOM	4364	CZ	TYR	A	581	17.171	29.144	22.583	1.00	50.66	A
ATOM	4365	OH	TYR	A	581	17.239	29.092	21.210	1.00	50.66	A
ATOM	4366	C	TYR	A	581	16.049	28.811	29.050	1.00	45.22	A
ATOM	4367	O	TYR	A	581	16.106	29.829	29.749	1.00	45.22	A
ATOM	4368	N	ILE	A	582	16.195	27.592	29.545	1.00	39.10	A
ATOM	4369	CA	ILE	A	582	16.486	27.397	30.960	1.00	39.10	A
ATOM	4370	CB	ILE	A	582	16.203	25.924	31.370	1.00	41.87	A
ATOM	4371	CG2	ILE	A	582	16.939	24.967	30.446	1.00	41.87	A
ATOM	4372	CG1	ILE	A	582	16.608	25.678	32.821	1.00	41.87	A
ATOM	4373	CD1	ILE	A	582	16.159	24.302	33.326	1.00	41.87	A
ATOM	4374	C	ILE	A	582	17.976	27.751	31.112	1.00	39.10	A
ATOM	4375	O	ILE	A	582	18.798	27.333	30.308	1.00	39.10	A
ATOM	4376	N	ARG	A	583	18.328	28.528	32.124	1.00	43.00	A
ATOM	4377	CA	ARG	A	583	19.731	28.909	32.279	1.00	43.00	A
ATOM	4378	CB	ARG	A	583	19.878	30.428	32.140	1.00	57.85	A
ATOM	4379	CG	ARG	A	583	18.911	31.025	31.134	1.00	57.85	A
ATOM	4380	CD	ARG	A	583	19.573	31.571	29.879	1.00	57.85	A
ATOM	4381	NE	ARG	A	583	20.420	30.619	29.168	1.00	57.85	A
ATOM	4382	CZ	ARG	A	583	20.704	30.709	27.866	1.00	57.85	A
ATOM	4383	NH1	ARG	A	583	20.195	31.696	27.143	1.00	57.85	A
ATOM	4384	NH2	ARG	A	583	21.528	29.838	27.293	1.00	57.85	A
ATOM	4385	C	ARG	A	583	20.348	28.465	33.595	1.00	43.00	A
ATOM	4386	O	ARG	A	583	21.500	28.036	33.624	1.00	43.00	A
ATOM	4387	N	LYS	A	584	19.579	28.561	34.677	1.00	44.21	A
ATOM	4388	CA	LYS	A	584	20.079	28.188	35.992	1.00	44.21	A
ATOM	4389	CB	LYS	A	584	20.504	29.450	36.749	1.00	51.60	A
ATOM	4390	CG	LYS	A	584	21.413	30.410	35.971	1.00	51.60	A
ATOM	4391	CD	LYS	A	584	22.796	29.849	35.715	1.00	51.60	A
ATOM	4392	CE	LYS	A	584	23.693	30.901	35.057	1.00	51.60	A
ATOM	4393	NZ	LYS	A	584	25.007	30.344	34.614	1.00	51.60	A
ATOM	4394	C	LYS	A	584	19.085	27.399	36.858	1.00	44.21	A
ATOM	4395	O	LYS	A	584	17.878	27.687	36.886	1.00	44.21	A
ATOM	4396	N	ILE	A	585	19.627	26.419	37.582	1.00	42.37	A
ATOM	4397	CA	ILE	A	585	18.870	25.565	38.489	1.00	42.37	A
ATOM	4398	CB	ILE	A	585	18.807	24.124	37.953	1.00	38.40	A
ATOM	4399	CG2	ILE	A	585	18.059	23.225	38.948	1.00	38.40	A
ATOM	4400	CG1	ILE	A	585	18.146	24.132	36.569	1.00	38.40	A
ATOM	4401	CD1	ILE	A	585	18.160	22.800	35.879	1.00	38.40	A
ATOM	4402	C	ILE	A	585	19.606	25.571	39.826	1.00	42.37	A
ATOM	4403	O	ILE	A	585	20.752	25.148	39.901	1.00	42.37	A
ATOM	4404	N	VAL	A	586	18.950	26.015	40.888	1.00	41.24	A
ATOM	4405	CA	VAL	A	586	19.631	26.090	42.175	1.00	41.24	A
ATOM	4406	CB	VAL	A	586	20.043	27.540	42.500	1.00	41.89	A
ATOM	4407	CG1	VAL	A	586	20.986	28.081	41.441	1.00	41.89	A
ATOM	4408	CG2	VAL	A	586	18.798	28.397	42.617	1.00	41.89	A
ATOM	4409	C	VAL	A	586	18.914	25.595	43.419	1.00	41.24	A
ATOM	4410	O	VAL	A	586	17.692	25.641	43.515	1.00	41.24	A
ATOM	4411	N	PRO	A	587	19.691	25.124	44.406	1.00	43.78	A
ATOM	4412	CD	PRO	A	587	21.128	24.818	44.331	1.00	58.45	A
ATOM	4413	CA	PRO	A	587	19.129	24.637	45.665	1.00	43.78	A
ATOM	4414	CB	PRO	A	587	20.219	23.709	46.213	1.00	58.45	A
ATOM	4415	CG	PRO	A	587	21.191	23.522	45.071	1.00	58.45	A
ATOM	4416	C	PRO	A	587	19.019	25.890	46.515	1.00	43.78	A
ATOM	4417	O	PRO	A	587	19.749	26.850	46.284	1.00	43.78	A
ATOM	4418	N	ILE	A	588	18.128	25.905	47.490	1.00	53.06	A
ATOM	4419	CA	ILE	A	588	18.027	27.080	48.328	1.00	53.06	A

FIGURE 25 CON'T

```
ATOM   4420  CB  ILE A 588      16.652  27.763  48.170  1.00 53.55      A
ATOM   4421  CG2 ILE A 588      16.546  28.980  49.090  1.00 53.55      A
ATOM   4422  CG1 ILE A 588      16.492  28.194  46.710  1.00 53.55      A
ATOM   4423  CD1 ILE A 588      15.412  29.187  46.476  1.00 53.55      A
ATOM   4424  C   ILE A 588      18.316  26.727  49.778  1.00 53.06      A
ATOM   4425  O   ILE A 588      17.439  26.299  50.539  1.00 53.06      A
ATOM   4426  N   LYS A 589      19.581  26.906  50.137  1.00 62.38      A
ATOM   4427  CA  LYS A 589      20.072  26.620  51.477  1.00 62.38      A
ATOM   4428  CB  LYS A 589      21.593  26.795  51.491  1.00 98.66      A
ATOM   4429  CG  LYS A 589      22.333  26.038  52.573  1.00 98.66      A
ATOM   4430  CD  LYS A 589      23.836  26.163  52.362  1.00 98.66      A
ATOM   4431  CE  LYS A 589      24.615  25.273  53.314  1.00 98.66      A
ATOM   4432  NZ  LYS A 589      24.361  25.631  54.734  1.00 98.66      A
ATOM   4433  C   LYS A 589      19.414  27.593  52.455  1.00 62.38      A
ATOM   4434  O   LYS A 589      19.259  28.773  52.152  1.00 62.38      A
ATOM   4435  N   ILE A 590      18.998  27.090  53.612  1.00 72.19      A
ATOM   4436  CA  ILE A 590      18.379  27.934  54.628  1.00 72.19      A
ATOM   4437  CB  ILE A 590      16.836  27.921  54.540  1.00 70.84      A
ATOM   4438  CG2 ILE A 590      16.387  28.396  53.168  1.00 70.84      A
ATOM   4439  CG1 ILE A 590      16.306  26.514  54.820  1.00 70.84      A
ATOM   4440  CD1 ILE A 590      14.797  26.441  54.917  1.00 70.84      A
ATOM   4441  C   ILE A 590      18.787  27.418  56.001  1.00 72.19      A
ATOM   4442  O   ILE A 590      19.033  26.225  56.171  1.00 72.19      A
ATOM   4443  N   GLY A 591      18.871  28.318  56.974  1.00 74.83      A
ATOM   4444  CA  GLY A 591      19.245  27.908  58.315  1.00 74.83      A
ATOM   4445  C   GLY A 591      18.101  27.164  58.978  1.00 74.83      A
ATOM   4446  O   GLY A 591      17.047  26.971  58.370  1.00 74.83      A
ATOM   4447  N   GLU A 592      18.304  26.740  60.222  1.00110.79      A
ATOM   4448  CA  GLU A 592      17.268  26.026  60.957  1.00110.79      A
ATOM   4449  CB  GLU A 592      17.799  25.558  62.314  1.00154.33      A
ATOM   4450  CG  GLU A 592      16.773  24.804  63.144  1.00154.33      A
ATOM   4451  CD  GLU A 592      17.318  24.356  64.484  1.00154.33      A
ATOM   4452  OE1 GLU A 592      17.770  25.220  65.264  1.00154.33      A
ATOM   4453  OE2 GLU A 592      17.291  23.138  64.758  1.00154.33      A
ATOM   4454  C   GLU A 592      16.065  26.941  61.160  1.00110.79      A
ATOM   4455  O   GLU A 592      16.218  28.121  61.476  1.00110.79      A
ATOM   4456  N   GLN A 593      14.870  26.389  60.981  1.00105.70      A
ATOM   4457  CA  GLN A 593      13.642  27.158  61.126  1.00105.70      A
ATOM   4458  CB  GLN A 593      12.499  26.465  60.388  1.00172.39      A
ATOM   4459  CG  GLN A 593      12.853  26.007  58.992  1.00172.39      A
ATOM   4460  CD  GLN A 593      11.657  25.464  58.245  1.00172.39      A
ATOM   4461  OE1 GLN A 593      10.979  24.546  58.710  1.00172.39      A
ATOM   4462  NE2 GLN A 593      11.389  26.030  57.078  1.00172.39      A
ATOM   4463  C   GLN A 593      13.243  27.347  62.581  1.00105.70      A
ATOM   4464  O   GLN A 593      13.261  26.400  63.366  1.00105.70      A
ATOM   4465  N   ARG A 594      12.877  28.577  62.931  1.00112.07      A
ATOM   4466  CA  ARG A 594      12.452  28.887  64.289  1.00112.07      A
ATOM   4467  CB  ARG A 594      12.507  30.397  64.534  1.00153.19      A
ATOM   4468  CG  ARG A 594      13.915  30.955  64.660  1.00153.19      A
ATOM   4469  CD  ARG A 594      14.653  30.313  65.827  1.00153.19      A
ATOM   4470  NE  ARG A 594      15.966  30.911  66.051  1.00153.19      A
ATOM   4471  CZ  ARG A 594      16.160  32.179  66.401  1.00153.19      A
ATOM   4472  NH1 ARG A 594      15.123  32.990  66.569  1.00153.19      A
ATOM   4473  NH2 ARG A 594      17.391  32.637  66.587  1.00153.19      A
ATOM   4474  C   ARG A 594      11.031  28.377  64.496  1.00112.07      A
ATOM   4475  O   ARG A 594      10.823  27.325  65.102  1.00112.07      A
ATOM   4476  N   GLY A 595      10.056  29.125  63.989  1.00111.54      A
```

FIGURE 25 CON'T

```
ATOM   4477  CA  GLY A 595       8.670  28.715  64.124  1.00111.54      A
ATOM   4478  C   GLY A 595       8.327  27.654  63.097  1.00111.54      A
ATOM   4479  O   GLY A 595       9.098  27.413  62.169  1.00111.54      A
ATOM   4480  N   GLU A 596       7.177  27.008  63.261  1.00136.15      A
ATOM   4481  CA  GLU A 596       6.756  25.978  62.320  1.00136.15      A
ATOM   4482  CB  GLU A 596       5.620  25.139  62.916  1.00144.37      A
ATOM   4483  CG  GLU A 596       6.072  24.148  63.984  1.00144.37      A
ATOM   4484  CD  GLU A 596       6.946  23.037  63.422  1.00144.37      A
ATOM   4485  OE1 GLU A 596       6.460  22.274  62.561  1.00144.37      A
ATOM   4486  OE2 GLU A 596       8.117  22.925  63.841  1.00144.37      A
ATOM   4487  C   GLU A 596       6.306  26.621  61.014  1.00136.15      A
ATOM   4488  O   GLU A 596       5.124  26.602  60.668  1.00136.15      A
ATOM   4489  N   SER A 597       7.269  27.193  60.297  1.00115.88      A
ATOM   4490  CA  SER A 597       7.016  27.857  59.024  1.00115.88      A
ATOM   4491  CB  SER A 597       6.091  29.057  59.227  1.00 95.41      A
ATOM   4492  OG  SER A 597       5.873  29.737  58.005  1.00 95.41      A
ATOM   4493  C   SER A 597       8.336  28.324  58.420  1.00115.88      A
ATOM   4494  O   SER A 597       9.210  28.825  59.129  1.00115.88      A
ATOM   4495  N   VAL A 598       8.479  28.157  57.109  1.00 68.76      A
ATOM   4496  CA  VAL A 598       9.701  28.560  56.419  1.00 68.76      A
ATOM   4497  CB  VAL A 598       9.765  27.967  54.994  1.00 80.99      A
ATOM   4498  CG1 VAL A 598      11.110  28.287  54.359  1.00 80.99      A
ATOM   4499  CG2 VAL A 598       9.529  26.467  55.040  1.00 80.99      A
ATOM   4500  C   VAL A 598       9.786  30.078  56.301  1.00 68.76      A
ATOM   4501  O   VAL A 598       8.816  30.728  55.912  1.00 68.76      A
ATOM   4502  N   ASP A 599      10.945  30.640  56.638  1.00 53.04      A
ATOM   4503  CA  ASP A 599      11.143  32.086  56.545  1.00 53.04      A
ATOM   4504  CB  ASP A 599      12.340  32.528  57.392  1.00 72.22      A
ATOM   4505  CG  ASP A 599      12.561  34.032  57.343  1.00 72.22      A
ATOM   4506  OD1 ASP A 599      12.782  34.574  56.241  1.00 72.22      A
ATOM   4507  OD2 ASP A 599      12.509  34.678  58.406  1.00 72.22      A

ATOM   4508  C   ASP A 599      11.386  32.462  55.087  1.00 53.04      A
ATOM   4509  O   ASP A 599      12.518  32.393  54.589  1.00 53.04      A
ATOM   4510  N   MSE A 600      10.323  32.878  54.408  1.00 59.23      A
ATOM   4511  CA  MSE A 600      10.425  33.230  53.003  1.00 59.23      A
ATOM   4512  CB  MSE A 600       9.028  33.456  52.423  1.00 57.98      A
ATOM   4513  CG  MSE A 600       8.137  32.205  52.487  1.00 57.98      A
ATOM   4514  SE  MSE A 600       9.060  30.559  51.959  1.00 57.98      A
ATOM   4515  CE  MSE A 600       9.289  30.938  50.077  1.00 57.98      A
ATOM   4516  C   MSE A 600      11.343  34.416  52.722  1.00 59.23      A
ATOM   4517  O   MSE A 600      11.885  34.536  51.617  1.00 59.23      A
ATOM   4518  N   ASN A 601      11.538  35.287  53.710  1.00 51.21      A
ATOM   4519  CA  ASN A 601      12.439  36.419  53.509  1.00 51.21      A
ATOM   4520  CB  ASN A 601      12.405  37.363  54.714  1.00 78.56      A
ATOM   4521  CG  ASN A 601      11.075  38.079  54.854  1.00 78.56      A
ATOM   4522  OD1 ASN A 601      10.591  38.699  53.909  1.00 78.56      A
ATOM   4523  ND2 ASN A 601      10.478  37.998  56.037  1.00 78.56      A
ATOM   4524  C   ASN A 601      13.836  35.842  53.319  1.00 51.21      A
ATOM   4525  O   ASN A 601      14.568  36.230  52.407  1.00 51.21      A
ATOM   4526  N   GLU A 602      14.190  34.885  54.168  1.00 50.53      A
ATOM   4527  CA  GLU A 602      15.499  34.238  54.087  1.00 50.53      A
ATOM   4528  CB  GLU A 602      15.696  33.313  55.291  1.00 60.76      A
ATOM   4529  CG  GLU A 602      17.076  32.672  55.381  1.00 60.76      A
ATOM   4530  CD  GLU A 602      17.148  31.600  56.455  1.00 60.76      A
ATOM   4531  OE1 GLU A 602      16.220  31.533  57.287  1.00 60.76      A
ATOM   4532  OE2 GLU A 602      18.131  30.831  56.472  1.00 60.76      A
```

FIGURE 25 CON'T

```
ATOM   4533  C   GLU A 602      15.579  33.424  52.792  1.00 50.53      A
ATOM   4534  O   GLU A 602      16.592  33.434  52.101  1.00 50.53      A
ATOM   4535  N   PHE A 603      14.490  32.729  52.475  1.00 50.35      A
ATOM   4536  CA  PHE A 603      14.403  31.898  51.277  1.00 50.35      A
ATOM   4537  CB  PHE A 603      12.987  31.302  51.178  1.00 52.94      A
ATOM   4538  CG  PHE A 603      12.818  30.288  50.075  1.00 52.94      A
ATOM   4539  CD1 PHE A 603      12.777  28.925  50.364  1.00 52.94      A
ATOM   4540  CD2 PHE A 603      12.687  30.692  48.750  1.00 52.94      A
ATOM   4541  CE1 PHE A 603      12.606  27.983  49.355  1.00 52.94      A
ATOM   4542  CE2 PHE A 603      12.515  29.749  47.727  1.00 52.94      A
ATOM   4543  CZ  PHE A 603      12.474  28.393  48.033  1.00 52.94      A
ATOM   4544  C   PHE A 603      14.725  32.689  50.003  1.00 50.35      A
ATOM   4545  O   PHE A 603      15.664  32.370  49.276  1.00 50.35      A
ATOM   4546  N   PHE A 604      13.940  33.722  49.729  1.00 46.12      A
ATOM   4547  CA  PHE A 604      14.152  34.524  48.537  1.00 46.12      A
ATOM   4548  CB  PHE A 604      12.981  35.500  48.353  1.00 50.73      A
ATOM   4549  CG  PHE A 604      11.672  34.816  48.010  1.00 50.73      A
ATOM   4550  CD1 PHE A 604      11.547  34.065  46.840  1.00 50.73      A
ATOM   4551  CD2 PHE A 604      10.574  34.910  48.857  1.00 50.73      A
ATOM   4552  CE1 PHE A 604      10.343  33.415  46.515  1.00 50.73      A
ATOM   4553  CE2 PHE A 604       9.368  34.262  48.542  1.00 50.73      A
ATOM   4554  CZ  PHE A 604       9.258  33.512  47.363  1.00 50.73      A
ATOM   4555  C   PHE A 604      15.496  35.256  48.559  1.00 46.12      A
ATOM   4556  O   PHE A 604      16.168  35.378  47.524  1.00 46.12      A
ATOM   4557  N   LYS A 605      15.909  35.728  49.729  1.00 56.20      A
ATOM   4558  CA  LYS A 605      17.194  36.409  49.807  1.00 56.20      A
ATOM   4559  CB  LYS A 605      17.469  36.883  51.240  1.00 83.58      A
ATOM   4560  CG  LYS A 605      18.801  37.594  51.407  1.00 83.58      A
ATOM   4561  CD  LYS A 605      18.921  38.256  52.777  1.00 83.58      A
ATOM   4562  CE  LYS A 605      20.381  38.484  53.161  1.00 83.58      A
ATOM   4563  NZ  LYS A 605      21.157  39.164  52.089  1.00 83.58      A
ATOM   4564  C   LYS A 605      18.263  35.416  49.344  1.00 56.20      A
ATOM   4565  O   LYS A 605      19.134  35.757  48.530  1.00 56.20      A
ATOM   4566  N   GLU A 606      18.189  34.182  49.846  1.00 44.36      A
ATOM   4567  CA  GLU A 606      19.157  33.172  49.427  1.00 44.36      A
ATOM   4568  CB  GLU A 606      18.997  31.885  50.236  1.00 58.25      A
ATOM   4569  CG  GLU A 606      19.884  30.744  49.730  1.00 58.25      A
ATOM   4570  CD  GLU A 606      21.359  31.118  49.680  1.00 58.25      A
ATOM   4571  OE1 GLU A 606      22.149  30.371  49.060  1.00 58.25      A
ATOM   4572  OE2 GLU A 606      21.734  32.159  50.262  1.00 58.25      A
ATOM   4573  C   GLU A 606      19.010  32.860  47.934  1.00 44.36      A
ATOM   4574  O   GLU A 606      19.998  32.566  47.253  1.00 44.36      A
ATOM   4575  N   MSE A 607      17.785  32.931  47.419  1.00 52.22      A
ATOM   4576  CA  MSE A 607      17.565  32.650  45.999  1.00 52.22      A
ATOM   4577  CB  MSE A 607      16.074  32.745  45.648  1.00 47.94      A
ATOM   4578  CG  MSE A 607      15.778  32.490  44.171  1.00 47.94      A
ATOM   4579  SE  MSE A 607      13.931  32.858  43.696  1.00 47.94      A
ATOM   4580  CE  MSE A 607      14.062  34.789  43.491  1.00 47.94      A
ATOM   4581  C   MSE A 607      18.353  33.651  45.159  1.00 52.22      A
ATOM   4582  O   MSE A 607      19.067  33.276  44.221  1.00 52.22      A
ATOM   4583  N   VAL A 608      18.216  34.929  45.507  1.00 49.17      A
ATOM   4584  CA  VAL A 608      18.917  35.996  44.804  1.00 49.17      A
ATOM   4585  CB  VAL A 608      18.492  37.375  45.342  1.00 62.97      A
ATOM   4586  CG1 VAL A 608      19.453  38.456  44.855  1.00 62.97      A
ATOM   4587  CG2 VAL A 608      17.091  37.686  44.867  1.00 62.97      A
ATOM   4588  C   VAL A 608      20.431  35.844  44.933  1.00 49.17      A
ATOM   4589  O   VAL A 608      21.162  35.933  43.945  1.00 49.17      A
```

FIGURE 25 CON'T

```
ATOM   4590  N   ASP A 609      20.902  35.600  46.148  1.00 54.49      A
ATOM   4591  CA  ASP A 609      22.333  35.433  46.366  1.00 54.49      A
ATOM   4592  CB  ASP A 609      22.641  35.350  47.862  1.00 60.18      A
ATOM   4593  CG  ASP A 609      22.438  36.673  48.573  1.00 60.18      A
ATOM   4594  OD1 ASP A 609      22.339  37.710  47.883  1.00 66.27      A
ATOM   4595  OD2 ASP A 609      22.378  36.675  49.821  1.00 66.27      A
ATOM   4596  C   ASP A 609      22.865  34.203  45.650  1.00 54.49      A
ATOM   4597  O   ASP A 609      23.970  34.228  45.096  1.00 54.49      A
ATOM   4598  N   LYS A 610      22.079  33.126  45.639  1.00 51.28      A
ATOM   4599  CA  LYS A 610      22.524  31.906  44.973  1.00 51.28      A
ATOM   4600  CB  LYS A 610      21.566  30.753  45.263  1.00 62.45      A
ATOM   4601  CG  LYS A 610      22.154  29.394  44.925  1.00 62.45      A
ATOM   4602  CD  LYS A 610      23.396  29.146  45.766  1.00 62.45      A
ATOM   4603  CE  LYS A 610      23.815  27.691  45.761  1.00 62.45      A
ATOM   4604  NZ  LYS A 610      24.296  27.265  44.431  1.00 62.45      A
ATOM   4605  C   LYS A 610      22.652  32.108  43.463  1.00 51.28      A
ATOM   4606  O   LYS A 610      23.611  31.641  42.848  1.00 51.28      A
ATOM   4607  N   PHE A 611      21.687  32.794  42.857  1.00 48.60      A
ATOM   4608  CA  PHE A 611      21.768  33.033  41.417  1.00 48.60      A
ATOM   4609  CB  PHE A 611      20.502  33.728  40.900  1.00 48.45      A
ATOM   4610  CG  PHE A 611      19.338  32.790  40.684  1.00 48.45      A
ATOM   4611  CD1 PHE A 611      19.473  31.669  39.867  1.00 48.45      A
ATOM   4612  CD2 PHE A 611      18.107  33.037  41.283  1.00 48.45      A
ATOM   4613  CE1 PHE A 611      18.392  30.799  39.646  1.00 48.45      A
ATOM   4614  CE2 PHE A 611      17.021  32.181  41.074  1.00 48.45      A
ATOM   4615  CZ  PHE A 611      17.163  31.055  40.251  1.00 48.45      A
ATOM   4616  C   PHE A 611      22.999  33.874  41.107  1.00 48.60      A
ATOM   4617  O   PHE A 611      23.663  33.672  40.085  1.00 48.60      A
ATOM   4618  N   LYS A 612      23.308  34.819  41.989  1.00 53.34      A
ATOM   4619  CA  LYS A 612      24.483  35.659  41.795  1.00 53.34      A
ATOM   4620  CB  LYS A 612      24.577  36.722  42.892  1.00 78.75      A
ATOM   4621  CG  LYS A 612      25.861  37.546  42.843  1.00 78.75      A
ATOM   4622  CD  LYS A 612      25.649  38.945  43.400  1.00 78.75      A
ATOM   4623  CE  LYS A 612      25.001  38.928  44.776  1.00 78.75      A
ATOM   4624  NZ  LYS A 612      25.831  38.201  45.778  1.00 78.75      A
ATOM   4625  C   LYS A 612      25.709  34.757  41.820  1.00 53.34      A
ATOM   4626  O   LYS A 612      26.601  34.888  40.987  1.00 53.34      A
ATOM   4627  N   GLU A 613      25.751  33.828  42.770  1.00 65.13      A
ATOM   4628  CA  GLU A 613      26.876  32.905  42.833  1.00 65.13      A
ATOM   4629  CB  GLU A 613      26.699  31.901  43.971  1.00101.27      A
ATOM   4630  CG  GLU A 613      27.889  30.965  44.133  1.00101.27      A
ATOM   4631  CD  GLU A 613      27.619  29.829  45.098  1.00101.27      A
ATOM   4632  OE1 GLU A 613      26.792  28.952  44.771  1.00101.27      A
ATOM   4633  OE2 GLU A 613      28.233  29.812  46.184  1.00101.27      A
ATOM   4634  C   GLU A 613      26.944  32.156  41.503  1.00 65.13      A
ATOM   4635  O   GLU A 613      28.019  31.738  41.073  1.00 65.13      A

ATOM   4636  N   PHE A 614      25.788  31.986  40.855  1.00 53.55      A
ATOM   4637  CA  PHE A 614      25.733  31.292  39.573  1.00 53.55      A
ATOM   4638  CB  PHE A 614      24.434  30.486  39.446  1.00 68.97      A
ATOM   4639  CG  PHE A 614      24.501  29.118  40.065  1.00 68.97      A
ATOM   4640  CD1 PHE A 614      23.759  28.068  39.531  1.00 68.97      A
ATOM   4641  CD2 PHE A 614      25.297  28.876  41.182  1.00 68.97      A
ATOM   4642  CE1 PHE A 614      23.810  26.793  40.102  1.00 68.97      A
ATOM   4643  CE2 PHE A 614      25.356  27.606  41.761  1.00 68.97      A
ATOM   4644  CZ  PHE A 614      24.612  26.563  41.221  1.00 68.97      A
ATOM   4645  C   PHE A 614      25.889  32.201  38.352  1.00 53.55      A
```

FIGURE 25 CON'T

ATOM	4646	O	PHE	A	614	25.631	31.769	37.224	1.00 53.55	A
ATOM	4647	N	ASN	A	615	26.301	33.453	38.584	1.00 55.93	A
ATOM	4648	CA	ASN	A	615	26.546	34.437	37.518	1.00 55.93	A
ATOM	4649	CB	ASN	A	615	27.310	33.784	36.361	1.00101.28	A
ATOM	4650	CG	ASN	A	615	28.714	33.380	36.749	1.00101.28	A
ATOM	4651	OD1	ASN	A	615	29.534	34.221	37.117	1.00101.28	A
ATOM	4652	ND2	ASN	A	615	29.001	32.084	36.672	1.00101.28	A
ATOM	4653	C	ASN	A	615	25.349	35.199	36.950	1.00 55.93	A
ATOM	4654	O	ASN	A	615	25.380	35.645	35.803	1.00 55.93	A
ATOM	4655	N	ILE	A	616	24.306	35.365	37.752	1.00 50.52	A
ATOM	4656	CA	ILE	A	616	23.120	36.088	37.313	1.00 50.52	A
ATOM	4657	CB	ILE	A	616	21.991	35.115	36.873	1.00 47.84	A
ATOM	4658	CG2	ILE	A	616	20.667	35.856	36.797	1.00 47.84	A
ATOM	4659	CG1	ILE	A	616	22.333	34.476	35.527	1.00 47.84	A
ATOM	4660	CD1	ILE	A	616	22.217	35.411	34.334	1.00 47.84	A
ATOM	4661	C	ILE	A	616	22.596	36.955	38.450	1.00 50.52	A
ATOM	4662	O	ILE	A	616	22.113	36.444	39.461	1.00 50.52	A
ATOM	4663	N	LYS	A	617	22.690	38.268	38.281	1.00 52.27	A
ATOM	4664	CA	LYS	A	617	22.207	39.197	39.298	1.00 52.27	A
ATOM	4665	CB	LYS	A	617	23.088	40.446	39.351	1.00 72.78	A
ATOM	4666	CG	LYS	A	617	24.537	40.152	39.673	1.00 72.78	A
ATOM	4667	CD	LYS	A	617	25.337	41.431	39.836	1.00 72.78	A
ATOM	4668	CE	LYS	A	617	26.793	41.122	40.127	1.00 72.78	A
ATOM	4669	NZ	LYS	A	617	27.532	42.345	40.532	1.00 72.78	A
ATOM	4670	C	LYS	A	617	20.780	39.590	38.960	1.00 52.27	A
ATOM	4671	O	LYS	A	617	20.507	40.061	37.851	1.00 52.27	A
ATOM	4672	N	LEU	A	618	19.876	39.394	39.915	1.00 66.85	A
ATOM	4673	CA	LEU	A	618	18.468	39.711	39.719	1.00 66.85	A
ATOM	4674	CB	LEU	A	618	17.592	38.782	40.565	1.00 47.81	A
ATOM	4675	CG	LEU	A	618	17.528	37.314	40.129	1.00 47.81	A
ATOM	4676	CD1	LEU	A	618	16.642	36.525	41.082	1.00 47.81	A
ATOM	4677	CD2	LEU	A	618	16.992	37.240	38.712	1.00 47.81	A
ATOM	4678	C	LEU	A	618	18.109	41.159	40.040	1.00 66.85	A
ATOM	4679	O	LEU	A	618	17.276	41.765	39.355	1.00 66.85	A
ATOM	4680	N	ASP	A	619	18.727	41.709	41.080	1.00100.67	A
ATOM	4681	CA	ASP	A	619	18.438	43.079	41.480	1.00100.67	A
ATOM	4682	CB	ASP	A	619	19.350	43.504	42.640	1.00105.68	A
ATOM	4683	CG	ASP	A	619	20.817	43.366	42.322	1.00105.68	A
ATOM	4684	OD1	ASP	A	619	21.225	42.301	41.815	1.00105.68	A
ATOM	4685	OD2	ASP	A	619	21.565	44.325	42.600	1.00105.68	A
ATOM	4686	C	ASP	A	619	18.546	44.053	40.313	1.00100.67	A
ATOM	4687	O	ASP	A	619	19.528	44.045	39.575	1.00100.67	A
ATOM	4688	N	ASN	A	620	17.500	44.866	40.158	1.00 62.07	A
ATOM	4689	CA	ASN	A	620	17.363	45.876	39.106	1.00 62.07	A
ATOM	4690	CB	ASN	A	620	18.731	46.458	38.718	1.00162.12	A
ATOM	4691	CG	ASN	A	620	19.295	45.848	37.444	1.00162.12	A
ATOM	4692	OD1	ASN	A	620	19.428	44.629	37.326	1.00162.12	A
ATOM	4693	ND2	ASN	A	620	19.635	46.700	36.483	1.00162.12	A
ATOM	4694	C	ASN	A	620	16.676	45.297	37.866	1.00 62.07	A
ATOM	4695	O	ASN	A	620	16.662	45.919	36.797	1.00 62.07	A
ATOM	4696	N	LYS	A	621	16.093	44.111	38.011	1.00 50.06	A
ATOM	4697	CA	LYS	A	621	15.437	43.459	36.882	1.00 50.06	A
ATOM	4698	CB	LYS	A	621	16.150	42.139	36.561	1.00 73.33	A
ATOM	4699	CG	LYS	A	621	17.613	42.287	36.174	1.00 73.33	A
ATOM	4700	CD	LYS	A	621	17.766	43.143	34.930	1.00 73.33	A
ATOM	4701	CE	LYS	A	621	19.204	43.184	34.439	1.00 73.33	A
ATOM	4702	NZ	LYS	A	621	19.649	41.849	33.963	1.00 73.33	A

FIGURE 25 CON'T

ATOM	4703	C	LYS	A	621	13.946	43.195	37.078	1.00	50.06	A
ATOM	4704	O	LYS	A	621	13.397	43.347	38.175	1.00	50.06	A
ATOM	4705	N	LYS	A	622	13.295	42.817	35.985	1.00	42.86	A
ATOM	4706	CA	LYS	A	622	11.876	42.505	36.006	1.00	42.86	A
ATOM	4707	CB	LYS	A	622	11.144	43.230	34.874	1.00	63.93	A
ATOM	4708	CG	LYS	A	622	9.641	43.076	34.944	1.00	63.93	A
ATOM	4709	CD	LYS	A	622	8.949	43.636	33.708	1.00	63.93	A
ATOM	4710	CE	LYS	A	622	7.442	43.438	33.811	1.00	63.93	A
ATOM	4711	NZ	LYS	A	622	6.714	43.798	32.561	1.00	63.93	A
ATOM	4712	C	LYS	A	622	11.738	40.992	35.833	1.00	42.86	A
ATOM	4713	O	LYS	A	622	12.228	40.419	34.849	1.00	42.86	A
ATOM	4714	N	ILE	A	623	11.088	40.351	36.799	1.00	45.44	A
ATOM	4715	CA	ILE	A	623	10.904	38.909	36.745	1.00	45.44	A
ATOM	4716	CB	ILE	A	623	11.811	38.180	37.765	1.00	48.09	A
ATOM	4717	CG2	ILE	A	623	13.272	38.577	37.555	1.00	48.09	A
ATOM	4718	CG1	ILE	A	623	11.369	38.531	39.187	1.00	48.09	A
ATOM	4719	CD1	ILE	A	623	12.147	37.821	40.266	1.00	48.09	A
ATOM	4720	C	ILE	A	623	9.475	38.469	37.036	1.00	45.44	A
ATOM	4721	O	ILE	A	623	8.725	39.143	37.746	1.00	45.44	A
ATOM	4722	N	LEU	A	624	9.124	37.322	36.463	1.00	46.63	A
ATOM	4723	CA	LEU	A	624	7.833	36.686	36.668	1.00	46.63	A
ATOM	4724	CB	LEU	A	624	7.298	36.129	35.351	1.00	41.36	A
ATOM	4725	CG	LEU	A	624	6.007	35.314	35.418	1.00	41.36	A
ATOM	4726	CD1	LEU	A	624	4.880	36.147	36.026	1.00	41.36	A
ATOM	4727	CD2	LEU	A	624	5.637	34.865	34.004	1.00	41.36	A
ATOM	4728	C	LEU	A	624	8.207	35.534	37.594	1.00	46.63	A
ATOM	4729	O	LEU	A	624	9.013	34.676	37.226	1.00	46.63	A
ATOM	4730	N	LEU	A	625	7.664	35.526	38.803	1.00	44.26	A
ATOM	4731	CA	LEU	A	625	7.989	34.458	39.734	1.00	44.26	A
ATOM	4732	CB	LEU	A	625	8.459	35.022	41.081	1.00	50.85	A
ATOM	4733	CG	LEU	A	625	9.043	33.954	42.015	1.00	50.85	A
ATOM	4734	CD1	LEU	A	625	10.317	34.478	42.652	1.00	50.85	A
ATOM	4735	CD2	LEU	A	625	8.019	33.550	43.066	1.00	50.85	A
ATOM	4736	C	LEU	A	625	6.742	33.634	39.918	1.00	44.26	A
ATOM	4737	O	LEU	A	625	5.671	34.181	40.157	1.00	44.26	A
ATOM	4738	N	LEU	A	626	6.891	32.320	39.808	1.00	40.96	A
ATOM	4739	CA	LEU	A	626	5.764	31.397	39.924	1.00	40.96	A
ATOM	4740	CB	LEU	A	626	5.357	30.906	38.530	1.00	38.76	A
ATOM	4741	CG	LEU	A	626	5.013	31.974	37.479	1.00	38.76	A
ATOM	4742	CD1	LEU	A	626	4.713	31.322	36.124	1.00	38.76	A
ATOM	4743	CD2	LEU	A	626	3.813	32.783	37.967	1.00	38.76	A
ATOM	4744	C	LEU	A	626	6.080	30.188	40.793	1.00	40.96	A
ATOM	4745	O	LEU	A	626	7.239	29.781	40.927	1.00	40.96	A
ATOM	4746	N	ARG	A	627	5.033	29.606	41.361	1.00	44.05	A
ATOM	4747	CA	ARG	A	627	5.158	28.424	42.203	1.00	44.05	A
ATOM	4748	CB	ARG	A	627	5.131	28.834	43.680	1.00	58.33	A
ATOM	4749	CG	ARG	A	627	3.786	29.349	44.165	1.00	58.33	A
ATOM	4750	CD	ARG	A	627	3.082	28.296	45.012	1.00	58.33	A
ATOM	4751	NE	ARG	A	627	3.619	28.237	46.371	1.00	58.33	A
ATOM	4752	CZ	ARG	A	627	3.726	27.125	47.098	1.00	58.33	A
ATOM	4753	NH1	ARG	A	627	3.341	25.951	46.602	1.00	58.33	A
ATOM	4754	NH2	ARG	A	627	4.206	27.189	48.336	1.00	58.33	A
ATOM	4755	C	ARG	A	627	3.978	27.494	41.884	1.00	44.05	A
ATOM	4756	O	ARG	A	627	3.058	27.882	41.162	1.00	44.05	A
ATOM	4757	N	ASP	A	628	4.020	26.270	42.401	1.00	44.99	A
ATOM	4758	CA	ASP	A	628	2.945	25.302	42.193	1.00	44.99	A
ATOM	4759	CB	ASP	A	628	3.445	23.876	42.469	1.00	51.65	A

FIGURE 25 CON'T

```
ATOM   4760  CG  ASP A 628       2.382  22.799  42.193  1.00 51.65      A
ATOM   4761  OD1 ASP A 628       1.169  23.090  42.242  1.00 51.65      A
ATOM   4762  OD2 ASP A 628       2.771  21.642  41.941  1.00 51.65      A
ATOM   4763  C   ASP A 628       1.817  25.628  43.167  1.00 44.99      A

ATOM   4764  O   ASP A 628       1.857  25.212  44.325  1.00 44.99      A
ATOM   4765  N   GLY A 629       0.817  26.370  42.703  1.00 45.09      A
ATOM   4766  CA  GLY A 629      -0.297  26.705  43.566  1.00 45.09      A
ATOM   4767  C   GLY A 629      -0.450  28.184  43.880  1.00 45.09      A
ATOM   4768  O   GLY A 629       0.061  29.051  43.157  1.00 45.09      A
ATOM   4769  N   ARG A 630      -1.142  28.471  44.976  1.00 58.81      A
ATOM   4770  CA  ARG A 630      -1.384  29.845  45.380  1.00 58.81      A
ATOM   4771  CB  ARG A 630      -2.609  29.902  46.298  1.00105.79      A
ATOM   4772  CG  ARG A 630      -3.080  31.311  46.619  1.00105.79      A
ATOM   4773  CD  ARG A 630      -4.225  31.306  47.619  1.00105.79      A
ATOM   4774  NE  ARG A 630      -3.816  30.714  48.888  1.00105.79      A
ATOM   4775  CZ  ARG A 630      -4.628  30.520  49.921  1.00105.79      A
ATOM   4776  NH1 ARG A 630      -5.904  30.872  49.842  1.00105.79      A
ATOM   4777  NH2 ARG A 630      -4.163  29.966  51.033  1.00105.79      A
ATOM   4778  C   ARG A 630      -0.184  30.486  46.077  1.00 58.81      A
ATOM   4779  O   ARG A 630       0.557  29.825  46.803  1.00 58.81      A
ATOM   4780  N   ILE A 631       0.012  31.777  45.827  1.00 52.71      A
ATOM   4781  CA  ILE A 631       1.086  32.532  46.464  1.00 52.71      A
ATOM   4782  CB  ILE A 631       1.327  33.881  45.748  1.00 62.65      A
ATOM   4783  CG2 ILE A 631       2.466  34.640  46.426  1.00 62.65      A
ATOM   4784  CG1 ILE A 631       1.612  33.644  44.261  1.00 62.65      A
ATOM   4785  CD1 ILE A 631       2.805  32.762  43.995  1.00 62.65      A
ATOM   4786  C   ILE A 631       0.605  32.827  47.889  1.00 52.71      A
ATOM   4787  O   ILE A 631      -0.390  33.516  48.071  1.00 52.71      A
ATOM   4788  N   THR A 632       1.304  32.308  48.893  1.00 47.14      A
ATOM   4789  CA  THR A 632       0.914  32.533  50.288  1.00 47.14      A
ATOM   4790  CB  THR A 632       1.645  31.563  51.237  1.00 53.31      A
ATOM   4791  OG1 THR A 632       3.047  31.864  51.221  1.00 53.31      A
ATOM   4792  CG2 THR A 632       1.433  30.108  50.807  1.00 53.31      A
ATOM   4793  C   THR A 632       1.248  33.959  50.753  1.00 47.14      A
ATOM   4794  O   THR A 632       2.007  34.685  50.097  1.00 47.14      A
ATOM   4795  N   ASN A 633       0.686  34.344  51.896  1.00 59.80      A
ATOM   4796  CA  ASN A 633       0.940  35.666  52.455  1.00 59.80      A
ATOM   4797  CB  ASN A 633       0.122  35.877  53.731  1.00 86.65      A
ATOM   4798  CG  ASN A 633      -1.370  35.813  53.480  1.00 86.65      A
ATOM   4799  OD1 ASN A 633      -1.874  36.395  52.517  1.00 86.65      A
ATOM   4800  ND2 ASN A 633      -2.089  35.111  54.350  1.00 86.65      A
ATOM   4801  C   ASN A 633       2.424  35.794  52.762  1.00 59.80      A
ATOM   4802  O   ASN A 633       3.041  36.825  52.479  1.00 59.80      A
ATOM   4803  N   ASN A 634       2.992  34.736  53.334  1.00 51.78      A
ATOM   4804  CA  ASN A 634       4.410  34.717  53.669  1.00 51.78      A
ATOM   4805  CB  ASN A 634       4.762  33.434  54.432  1.00 64.55      A
ATOM   4806  CG  ASN A 634       4.318  33.478  55.886  1.00 64.55      A
ATOM   4807  OD1 ASN A 634       3.706  34.453  56.335  1.00 64.55      A
ATOM   4808  ND2 ASN A 634       4.628  32.421  56.629  1.00 64.55      A
ATOM   4809  C   ASN A 634       5.277  34.821  52.423  1.00 51.78      A
ATOM   4810  O   ASN A 634       6.350  35.432  52.455  1.00 51.78      A
ATOM   4811  N   GLU A 635       4.828  34.224  51.322  1.00 53.86      A
ATOM   4812  CA  GLU A 635       5.606  34.292  50.093  1.00 53.86      A
ATOM   4813  CB  GLU A 635       5.140  33.226  49.098  1.00 57.25      A
ATOM   4814  CG  GLU A 635       5.447  31.815  49.584  1.00 57.25      A
ATOM   4815  CD  GLU A 635       4.832  30.732  48.720  1.00 57.25      A
```

FIGURE 25 CON'T

ATOM	4816	OE1	GLU	A	635	3.652	30.872	48.345	1.00	57.25	A
ATOM	4817	OE2	GLU	A	635	5.527	29.736	48.429	1.00	57.25	A
ATOM	4818	C	GLU	A	635	5.513	35.685	49.498	1.00	53.86	A
ATOM	4819	O	GLU	A	635	6.471	36.174	48.900	1.00	53.86	A
ATOM	4820	N	GLU	A	636	4.371	36.335	49.678	1.00	53.88	A
ATOM	4821	CA	GLU	A	636	4.216	37.688	49.169	1.00	53.88	A
ATOM	4822	CB	GLU	A	636	2.764	38.154	49.296	1.00	73.18	A
ATOM	4823	CG	GLU	A	636	2.536	39.571	48.792	1.00	73.18	A
ATOM	4824	CD	GLU	A	636	1.073	39.954	48.759	1.00	73.18	A
ATOM	4825	OE1	GLU	A	636	0.340	39.440	47.890	1.00	73.18	A
ATOM	4826	OE2	GLU	A	636	0.656	40.768	49.607	1.00	73.18	A
ATOM	4827	C	GLU	A	636	5.142	38.603	49.979	1.00	53.88	A
ATOM	4828	O	GLU	A	636	5.880	39.414	49.412	1.00	53.88	A
ATOM	4829	N	GLU	A	637	5.116	38.458	51.301	1.00	60.42	A
ATOM	4830	CA	GLU	A	637	5.978	39.263	52.165	1.00	60.42	A
ATOM	4831	CB	GLU	A	637	5.847	38.838	53.630	1.00	135.81	A
ATOM	4832	CG	GLU	A	637	4.536	39.200	54.291	1.00	135.81	A
ATOM	4833	CD	GLU	A	637	4.569	38.962	55.788	1.00	135.81	A
ATOM	4834	OE1	GLU	A	637	4.805	37.807	56.200	1.00	135.81	A
ATOM	4835	OE2	GLU	A	637	4.365	39.930	56.551	1.00	135.81	A
ATOM	4836	C	GLU	A	637	7.416	39.057	51.729	1.00	60.42	A
ATOM	4837	O	GLU	A	637	8.153	40.015	51.471	1.00	60.42	A
ATOM	4838	N	GLY	A	638	7.804	37.786	51.656	1.00	47.17	A
ATOM	4839	CA	GLY	A	638	9.149	37.443	51.250	1.00	47.17	A
ATOM	4840	C	GLY	A	638	9.479	38.087	49.927	1.00	47.17	A
ATOM	4841	O	GLY	A	638	10.621	38.474	49.697	1.00	47.17	A
ATOM	4842	N	LEU	A	639	8.487	38.204	49.050	1.00	49.32	A
ATOM	4843	CA	LEU	A	639	8.719	38.819	47.744	1.00	49.32	A
ATOM	4844	CB	LEU	A	639	7.638	38.387	46.749	1.00	56.98	A
ATOM	4845	CG	LEU	A	639	7.688	36.923	46.308	1.00	56.98	A
ATOM	4846	CD1	LEU	A	639	6.629	36.690	45.251	1.00	56.98	A
ATOM	4847	CD2	LEU	A	639	9.060	36.595	45.743	1.00	56.98	A
ATOM	4848	C	LEU	A	639	8.786	40.351	47.833	1.00	49.32	A
ATOM	4849	O	LEU	A	639	9.463	40.999	47.029	1.00	49.32	A
ATOM	4850	N	LYS	A	640	8.079	40.933	48.795	1.00	68.00	A
ATOM	4851	CA	LYS	A	640	8.131	42.379	48.966	1.00	68.00	A
ATOM	4852	CB	LYS	A	640	7.088	42.850	49.991	1.00	63.26	A
ATOM	4853	CG	LYS	A	640	5.640	42.688	49.529	1.00	63.26	A
ATOM	4854	CD	LYS	A	640	4.654	43.472	50.402	1.00	63.26	A
ATOM	4855	CE	LYS	A	640	4.583	42.949	51.832	1.00	63.26	A
ATOM	4856	NZ	LYS	A	640	3.587	43.707	52.654	1.00	63.26	A
ATOM	4857	C	LYS	A	640	9.541	42.683	49.472	1.00	68.00	A
ATOM	4858	O	LYS	A	640	10.181	43.653	49.059	1.00	68.00	A
ATOM	4859	N	TYR	A	641	10.019	41.810	50.354	1.00	68.42	A
ATOM	4860	CA	TYR	A	641	11.339	41.917	50.961	1.00	68.42	A
ATOM	4861	CB	TYR	A	641	11.549	40.711	51.874	1.00	67.22	A
ATOM	4862	CG	TYR	A	641	12.853	40.700	52.630	1.00	67.22	A
ATOM	4863	CD1	TYR	A	641	13.122	41.659	53.608	1.00	67.22	A
ATOM	4864	CE1	TYR	A	641	14.312	41.625	54.339	1.00	67.22	A
ATOM	4865	CD2	TYR	A	641	13.806	39.710	52.393	1.00	67.22	A
ATOM	4866	CE2	TYR	A	641	14.994	39.667	53.111	1.00	67.22	A
ATOM	4867	CZ	TYR	A	641	15.243	40.625	54.085	1.00	67.22	A
ATOM	4868	OH	TYR	A	641	16.416	40.580	54.806	1.00	67.22	A
ATOM	4869	C	TYR	A	641	12.453	41.983	49.912	1.00	68.42	A
ATOM	4870	O	TYR	A	641	13.265	42.906	49.897	1.00	68.42	A
ATOM	4871	N	ILE	A	642	12.475	40.985	49.038	1.00	56.35	A
ATOM	4872	CA	ILE	A	642	13.462	40.872	47.970	1.00	56.35	A

FIGURE 25 CON'T

```
ATOM   4873  CB  ILE A 642      13.351  39.460  47.329  1.00 86.15      A
ATOM   4874  CG2 ILE A 642      11.907  39.184  46.934  1.00 86.15      A
ATOM   4875  CG1 ILE A 642      14.264  39.330  46.116  1.00 86.15      A
ATOM   4876  CD1 ILE A 642      14.002  38.056  45.315  1.00 86.15      A
ATOM   4877  C   ILE A 642      13.278  41.967  46.905  1.00 56.35      A
ATOM   4878  O   ILE A 642      14.208  42.301  46.173  1.00 56.35      A
ATOM   4879  N   SER A 643      12.076  42.523  46.822  1.00 60.93      A
ATOM   4880  CA  SER A 643      11.786  43.572  45.846  1.00 60.93      A
ATOM   4881  CB  SER A 643      10.271  43.761  45.710  1.00 54.02      A
ATOM   4882  OG  SER A 643       9.945  44.827  44.830  1.00 54.02      A
ATOM   4883  C   SER A 643      12.432  44.893  46.256  1.00 60.93      A
ATOM   4884  O   SER A 643      13.083  45.553  45.444  1.00 60.93      A
ATOM   4885  N   GLU A 644      12.245  45.273  47.516  1.00 75.63      A
ATOM   4886  CA  GLU A 644      12.814  46.515  48.021  1.00 75.63      A
ATOM   4887  CB  GLU A 644      12.196  46.870  49.378  1.00159.47      A
ATOM   4888  CG  GLU A 644      12.866  48.046  50.082  1.00159.47      A
ATOM   4889  CD  GLU A 644      12.995  49.271  49.192  1.00159.47      A
ATOM   4890  OE1 GLU A 644      11.959  49.782  48.717  1.00159.47      A
ATOM   4891  OE2 GLU A 644      14.138  49.724  48.966  1.00159.47      A

ATOM   4892  C   GLU A 644      14.327  46.413  48.155  1.00 75.63      A
ATOM   4893  O   GLU A 644      15.068  47.231  47.605  1.00 75.63      A
ATOM   4894  N   MSE A 645      14.778  45.394  48.877  1.00 71.24      A
ATOM   4895  CA  MSE A 645      16.199  45.183  49.108  1.00 71.24      A
ATOM   4896  CB  MSE A 645      16.413  43.877  49.880  1.00 69.55      A
ATOM   4897  CG  MSE A 645      17.879  43.527  50.099  1.00 69.55      A
ATOM   4898  SE  MSE A 645      18.158  41.917  51.128  1.00 69.55      A
ATOM   4899  CE  MSE A 645      17.652  42.616  52.856  1.00 69.55      A
ATOM   4900  C   MSE A 645      17.050  45.169  47.840  1.00 71.24      A
ATOM   4901  O   MSE A 645      18.138  45.742  47.813  1.00 71.24      A
ATOM   4902  N   PHE A 646      16.554  44.524  46.789  1.00 51.49      A
ATOM   4903  CA  PHE A 646      17.306  44.414  45.544  1.00 51.49      A
ATOM   4904  CB  PHE A 646      17.384  42.941  45.128  1.00 57.55      A
ATOM   4905  CG  PHE A 646      18.132  42.071  46.096  1.00 57.55      A
ATOM   4906  CD1 PHE A 646      19.519  42.118  46.166  1.00 57.55      A
ATOM   4907  CD2 PHE A 646      17.445  41.210  46.950  1.00 57.55      A
ATOM   4908  CE1 PHE A 646      20.217  41.316  47.078  1.00 57.55      A
ATOM   4909  CE2 PHE A 646      18.126  40.408  47.861  1.00 57.55      A
ATOM   4910  CZ  PHE A 646      19.516  40.459  47.928  1.00 57.55      A
ATOM   4911  C   PHE A 646      16.734  45.218  44.386  1.00 51.49      A
ATOM   4912  O   PHE A 646      17.254  45.147  43.273  1.00 51.49      A
ATOM   4913  N   ASP A 647      15.673  45.981  44.633  1.00 57.02      A
ATOM   4914  CA  ASP A 647      15.039  46.755  43.562  1.00 57.02      A
ATOM   4915  CB  ASP A 647      15.992  47.828  43.012  1.00 72.79      A
ATOM   4916  CG  ASP A 647      16.262  48.941  44.010  1.00 72.79      A
ATOM   4917  OD1 ASP A 647      15.288  49.563  44.489  1.00 72.79      A
ATOM   4918  OD2 ASP A 647      17.447  49.196  44.310  1.00 72.79      A
ATOM   4919  C   ASP A 647      14.615  45.811  42.429  1.00 57.02      A
ATOM   4920  O   ASP A 647      14.929  46.026  41.254  1.00 57.02      A
ATOM   4921  N   ILE A 648      13.917  44.747  42.798  1.00 55.16      A
ATOM   4922  CA  ILE A 648      13.443  43.783  41.816  1.00 55.16      A
ATOM   4923  CB  ILE A 648      13.634  42.323  42.324  1.00 54.96      A
ATOM   4924  CG2 ILE A 648      13.066  41.326  41.302  1.00 54.96      A
ATOM   4925  CG1 ILE A 648      15.122  42.050  42.573  1.00 54.96      A
ATOM   4926  CD1 ILE A 648      15.404  40.717  43.254  1.00 54.96      A
ATOM   4927  C   ILE A 648      11.961  44.035  41.586  1.00 55.16      A
ATOM   4928  O   ILE A 648      11.195  44.126  42.542  1.00 55.16      A
```

FIGURE 25 CON'T

```
ATOM   4929  N   GLU A 649      11.562  44.184  40.328  1.00 43.65      A
ATOM   4930  CA  GLU A 649      10.147  44.379  40.013  1.00 43.65      A
ATOM   4931  CB  GLU A 649       9.971  45.137  38.696  1.00 74.80      A
ATOM   4932  CG  GLU A 649       8.520  45.475  38.389  1.00 74.80      A
ATOM   4933  CD  GLU A 649       8.316  46.079  37.006  1.00 74.80      A
ATOM   4934  OE1 GLU A 649       7.149  46.344  36.648  1.00 74.80      A
ATOM   4935  OE2 GLU A 649       9.309  46.290  36.275  1.00 74.80      A
ATOM   4936  C   GLU A 649       9.593  42.956  39.875  1.00 43.65      A
ATOM   4937  O   GLU A 649       9.868  42.270  38.889  1.00 43.65      A
ATOM   4938  N   VAL A 650       8.825  42.515  40.869  1.00 51.93      A
ATOM   4939  CA  VAL A 650       8.281  41.158  40.868  1.00 51.93      A
ATOM   4940  CB  VAL A 650       8.378  40.504  42.277  1.00 53.47      A
ATOM   4941  CG1 VAL A 650       8.045  39.018  42.181  1.00 53.47      A
ATOM   4942  CG2 VAL A 650       9.761  40.719  42.877  1.00 53.47      A
ATOM   4943  C   VAL A 650       6.833  40.997  40.440  1.00 51.93      A
ATOM   4944  O   VAL A 650       5.938  41.537  41.073  1.00 51.93      A
ATOM   4945  N   VAL A 651       6.605  40.239  39.372  1.00 46.48      A
ATOM   4946  CA  VAL A 651       5.244  39.955  38.927  1.00 46.48      A
ATOM   4947  CB  VAL A 651       5.070  40.116  37.398  1.00 47.71      A
ATOM   4948  CG1 VAL A 651       3.640  39.765  36.999  1.00 47.71      A
ATOM   4949  CG2 VAL A 651       5.388  41.537  36.978  1.00 47.71      A
ATOM   4950  C   VAL A 651       4.968  38.491  39.300  1.00 46.48      A
ATOM   4951  O   VAL A 651       5.795  37.603  39.046  1.00 46.48      A
ATOM   4952  N   THR A 652       3.818  38.240  39.916  1.00 49.59      A
ATOM   4953  CA  THR A 652       3.474  36.884  40.309  1.00 49.59      A
ATOM   4954  CB  THR A 652       4.056  36.552  41.709  1.00 46.75      A
ATOM   4955  OG1 THR A 652       3.934  35.145  41.959  1.00 46.75      A
ATOM   4956  CG2 THR A 652       3.314  37.319  42.798  1.00 46.75      A
ATOM   4957  C   THR A 652       1.967  36.691  40.317  1.00 49.59      A
ATOM   4958  O   THR A 652       1.214  37.661  40.237  1.00 49.59      A
ATOM   4959  N   MSE A 653       1.537  35.435  40.409  1.00 46.98      A
ATOM   4960  CA  MSE A 653       0.116  35.087  40.432  1.00 46.98      A
ATOM   4961  CB  MSE A 653      -0.491  35.262  39.035  1.00 57.38      A
ATOM   4962  CG  MSE A 653      -0.007  34.233  38.043  1.00 57.38      A
ATOM   4963  SE  MSE A 653      -0.624  34.530  36.245  1.00 57.38      A
ATOM   4964  CE  MSE A 653       0.932  35.480  35.569  1.00 57.38      A
ATOM   4965  C   MSE A 653      -0.077  33.630  40.871  1.00 46.98      A
ATOM   4966  O   MSE A 653       0.872  32.851  40.901  1.00 46.98      A
ATOM   4967  N   ASP A 654      -1.308  33.269  41.213  1.00 51.12      A
ATOM   4968  CA  ASP A 654      -1.613  31.897  41.607  1.00 51.12      A
ATOM   4969  CB  ASP A 654      -2.954  31.814  42.348  1.00 53.20      A
ATOM   4970  CG  ASP A 654      -2.953  32.565  43.673  1.00 53.20      A
ATOM   4971  OD1 ASP A 654      -1.868  32.770  44.272  1.00 53.20      A
ATOM   4972  OD2 ASP A 654      -4.060  32.930  44.128  1.00 53.20      A
ATOM   4973  C   ASP A 654      -1.709  31.022  40.354  1.00 51.12      A
ATOM   4974  O   ASP A 654      -2.436  31.355  39.416  1.00 51.12      A
ATOM   4975  N   VAL A 655      -0.964  29.918  40.335  1.00 44.06      A
ATOM   4976  CA  VAL A 655      -1.004  28.980  39.223  1.00 44.06      A
ATOM   4977  CB  VAL A 655       0.377  28.790  38.589  1.00 43.58      A
ATOM   4978  CG1 VAL A 655       0.286  27.774  37.468  1.00 43.58      A
ATOM   4979  CG2 VAL A 655       0.884  30.112  38.057  1.00 43.58      A
ATOM   4980  C   VAL A 655      -1.475  27.681  39.863  1.00 44.06      A
ATOM   4981  O   VAL A 655      -0.692  26.930  40.457  1.00 44.06      A
ATOM   4982  N   ILE A 656      -2.772  27.428  39.740  1.00 46.88      A
ATOM   4983  CA  ILE A 656      -3.392  26.276  40.368  1.00 46.88      A
ATOM   4984  CB  ILE A 656      -4.638  26.756  41.150  1.00 39.39      A
ATOM   4985  CG2 ILE A 656      -5.289  25.599  41.887  1.00 39.39      A
```

FIGURE 25 CON'T

```
ATOM   4986  CG1 ILE A 656      -4.222  27.850  42.137  1.00 39.39      A
ATOM   4987  CD1 ILE A 656      -5.385  28.702  42.646  1.00 39.39      A
ATOM   4988  C   ILE A 656      -3.766  25.140  39.420  1.00 46.88      A
ATOM   4989  O   ILE A 656      -4.572  25.310  38.498  1.00 46.88      A
ATOM   4990  N   LYS A 657      -3.176  23.976  39.665  1.00 42.94      A
ATOM   4991  CA  LYS A 657      -3.442  22.805  38.848  1.00 42.94      A
ATOM   4992  CB  LYS A 657      -2.150  22.009  38.604  1.00 49.37      A
ATOM   4993  CG  LYS A 657      -1.608  21.245  39.811  1.00 49.37      A
ATOM   4994  CD  LYS A 657      -0.314  20.513  39.435  1.00 49.37      A
ATOM   4995  CE  LYS A 657       0.054  19.413  40.436  1.00 49.37      A
ATOM   4996  NZ  LYS A 657       0.180  19.904  41.836  1.00 49.37      A
ATOM   4997  C   LYS A 657      -4.482  21.920  39.536  1.00 42.94      A
ATOM   4998  O   LYS A 657      -5.128  21.103  38.891  1.00 42.94      A
ATOM   4999  N   ASN A 658      -4.645  22.094  40.843  1.00 43.70      A
ATOM   5000  CA  ASN A 658      -5.600  21.295  41.594  1.00 43.70      A
ATOM   5001  CB  ASN A 658      -4.952  20.728  42.864  1.00 76.60      A
ATOM   5002  CG  ASN A 658      -3.824  19.754  42.560  1.00 76.60      A
ATOM   5003  OD1 ASN A 658      -3.961  18.871  41.711  1.00 76.60      A
ATOM   5004  ND2 ASN A 658      -2.705  19.907  43.262  1.00 76.60      A
ATOM   5005  C   ASN A 658      -6.833  22.089  41.962  1.00 43.70      A
ATOM   5006  O   ASN A 658      -6.875  22.780  42.974  1.00 43.70      A
ATOM   5007  N   HIS A 659      -7.844  21.977  41.118  1.00 37.49      A
ATOM   5008  CA  HIS A 659      -9.100  22.672  41.312  1.00 37.49      A
ATOM   5009  CB  HIS A 659      -9.046  24.038  40.602  1.00 35.90      A
ATOM   5010  CG  HIS A 659      -8.790  23.944  39.130  1.00 35.90      A
ATOM   5011  CD2 HIS A 659      -7.631  23.935  38.424  1.00 35.90      A
ATOM   5012  ND1 HIS A 659      -9.798  23.722  38.213  1.00 35.90      A
ATOM   5013  CE1 HIS A 659      -9.270  23.574  37.010  1.00 35.90      A
ATOM   5014  NE2 HIS A 659      -7.957  23.699  37.109  1.00 35.90      A
ATOM   5015  C   HIS A 659     -10.110  21.710  40.691  1.00 37.49      A
ATOM   5016  O   HIS A 659      -9.733  20.806  39.936  1.00 37.49      A
ATOM   5017  N   PRO A 660     -11.401  21.890  40.997  1.00 33.96      A
ATOM   5018  CD  PRO A 660     -11.929  22.848  41.994  1.00 33.10      A
ATOM   5019  CA  PRO A 660     -12.467  21.031  40.489  1.00 33.96      A

ATOM   5020  CB  PRO A 660     -13.427  21.002  41.662  1.00 33.10      A
ATOM   5021  CG  PRO A 660     -13.415  22.494  42.056  1.00 33.10      A
ATOM   5022  C   PRO A 660     -13.190  21.442  39.193  1.00 33.96      A
ATOM   5023  O   PRO A 660     -14.043  20.710  38.719  1.00 33.96      A
ATOM   5024  N   VAL A 661     -12.866  22.601  38.634  1.00 38.34      A
ATOM   5025  CA  VAL A 661     -13.550  23.073  37.435  1.00 38.34      A
ATOM   5026  CB  VAL A 661     -13.310  24.582  37.230  1.00 39.74      A
ATOM   5027  CG1 VAL A 661     -13.938  25.042  35.923  1.00 39.74      A
ATOM   5028  CG2 VAL A 661     -13.908  25.356  38.392  1.00 39.74      A
ATOM   5029  C   VAL A 661     -13.161  22.341  36.164  1.00 38.34      A
ATOM   5030  O   VAL A 661     -11.983  22.202  35.858  1.00 38.34      A
ATOM   5031  N   ARG A 662     -14.155  21.860  35.427  1.00 38.85      A
ATOM   5032  CA  ARG A 662     -13.895  21.147  34.172  1.00 38.85      A
ATOM   5033  CB  ARG A 662     -14.116  19.643  34.365  1.00 38.35      A
ATOM   5034  CG  ARG A 662     -13.129  18.981  35.351  1.00 38.35      A
ATOM   5035  CD  ARG A 662     -11.704  18.956  34.794  1.00 38.35      A
ATOM   5036  NE  ARG A 662     -10.762  18.319  35.712  1.00 38.35      A
ATOM   5037  CZ  ARG A 662     -10.229  18.908  36.782  1.00 38.35      A
ATOM   5038  NH1 ARG A 662     -10.531  20.165  37.080  1.00 38.35      A
ATOM   5039  NH2 ARG A 662      -9.411  18.226  37.567  1.00 38.35      A
ATOM   5040  C   ARG A 662     -14.786  21.652  33.032  1.00 38.85      A
ATOM   5041  O   ARG A 662     -15.963  21.953  33.250  1.00 38.85      A
```

FIGURE 25 CON'T

```
ATOM   5042  N   ALA A 663     -14.201  21.769  31.839  1.00 45.78      A
ATOM   5043  CA  ALA A 663     -14.920  22.196  30.628  1.00 45.78      A
ATOM   5044  CB  ALA A 663     -14.133  23.258  29.870  1.00 44.45      A
ATOM   5045  C   ALA A 663     -15.030  20.938  29.787  1.00 45.78      A
ATOM   5046  O   ALA A 663     -14.016  20.307  29.457  1.00 45.78      A
ATOM   5047  N   PHE A 664     -16.255  20.570  29.441  1.00 48.74      A
ATOM   5048  CA  PHE A 664     -16.479  19.347  28.685  1.00 48.74      A
ATOM   5049  CB  PHE A 664     -17.866  18.808  29.022  1.00 42.62      A
ATOM   5050  CG  PHE A 664     -18.045  18.505  30.480  1.00 42.62      A
ATOM   5051  CD1 PHE A 664     -17.025  17.870  31.199  1.00 42.62      A
ATOM   5052  CD2 PHE A 664     -19.224  18.826  31.133  1.00 42.62      A
ATOM   5053  CE1 PHE A 664     -17.186  17.560  32.550  1.00 42.62      A
ATOM   5054  CE2 PHE A 664     -19.397  18.520  32.483  1.00 42.62      A
ATOM   5055  CZ  PHE A 664     -18.372  17.884  33.194  1.00 42.62      A
ATOM   5056  C   PHE A 664     -16.274  19.402  27.175  1.00 48.74      A
ATOM   5057  O   PHE A 664     -17.210  19.226  26.390  1.00 48.74      A
ATOM   5058  N   ALA A 665     -15.027  19.638  26.786  1.00 51.15      A
ATOM   5059  CA  ALA A 665     -14.627  19.699  25.388  1.00 51.15      A
ATOM   5060  CB  ALA A 665     -14.886  21.103  24.810  1.00 44.63      A
ATOM   5061  C   ALA A 665     -13.138  19.391  25.370  1.00 51.15      A
ATOM   5062  O   ALA A 665     -12.421  19.763  26.296  1.00 51.15      A
ATOM   5063  N   ASN A 666     -12.671  18.701  24.336  1.00 53.36      A
ATOM   5064  CA  ASN A 666     -11.253  18.397  24.246  1.00 53.36      A
ATOM   5065  CB  ASN A 666     -11.030  16.927  23.878  1.00 54.17      A
ATOM   5066  CG  ASN A 666      -9.549  16.553  23.853  1.00 54.17      A
ATOM   5067  OD1 ASN A 666      -8.746  17.119  24.593  1.00 54.17      A
ATOM   5068  ND2 ASN A 666      -9.189  15.589  23.009  1.00 54.17      A
ATOM   5069  C   ASN A 666     -10.594  19.314  23.221  1.00 53.36      A
ATOM   5070  O   ASN A 666     -10.374  18.936  22.074  1.00 53.36      A
ATOM   5071  N   MSE A 667     -10.299  20.536  23.645  1.00 46.65      A
ATOM   5072  CA  MSE A 667      -9.653  21.513  22.779  1.00 46.65      A
ATOM   5073  CB  MSE A 667     -10.680  22.187  21.847  1.00 79.72      A
ATOM   5074  CG  MSE A 667     -11.765  23.012  22.549  1.00 79.72      A
ATOM   5075  SE  MSE A 667     -12.931  24.041  21.337  1.00 79.72      A
ATOM   5076  CE  MSE A 667     -12.819  25.765  22.187  1.00 79.72      A
ATOM   5077  C   MSE A 667      -8.951  22.584  23.606  1.00 46.65      A
ATOM   5078  O   MSE A 667      -9.263  22.783  24.778  1.00 46.65      A
ATOM   5079  N   LYS A 668      -8.005  23.269  22.975  1.00 56.56      A
ATOM   5080  CA  LYS A 668      -7.265  24.341  23.619  1.00 56.56      A
ATOM   5081  CB  LYS A 668      -6.034  24.702  22.785  1.00 74.88      A
ATOM   5082  CG  LYS A 668      -5.040  23.556  22.646  1.00 74.88      A
ATOM   5083  CD  LYS A 668      -3.838  23.949  21.800  1.00 74.88      A
ATOM   5084  CE  LYS A 668      -4.200  24.077  20.323  1.00 74.88      A
ATOM   5085  NZ  LYS A 668      -4.605  22.768  19.742  1.00 74.88      A
ATOM   5086  C   LYS A 668      -8.197  25.536  23.736  1.00 56.56      A
ATOM   5087  O   LYS A 668      -8.907  25.875  22.788  1.00 56.56      A
ATOM   5088  N   MSE A 669      -8.183  26.175  24.902  1.00 48.15      A
ATOM   5089  CA  MSE A 669      -9.049  27.314  25.176  1.00 48.15      A
ATOM   5090  CB  MSE A 669     -10.495  26.824  25.261  1.00 60.60      A
ATOM   5091  CG  MSE A 669     -10.694  25.792  26.376  1.00 60.60      A
ATOM   5092  SE  MSE A 669     -12.469  25.027  26.528  1.00 60.60      A
ATOM   5093  CE  MSE A 669     -13.075  26.047  27.994  1.00 60.60      A
ATOM   5094  C   MSE A 669      -8.680  27.962  26.510  1.00 48.15      A
ATOM   5095  O   MSE A 669      -7.782  27.509  27.210  1.00 48.15      A
ATOM   5096  N   TYR A 670      -9.394  29.025  26.849  1.00 45.94      A
ATOM   5097  CA  TYR A 670      -9.225  29.723  28.114  1.00 45.94      A
ATOM   5098  CB  TYR A 670      -7.957  30.586  28.112  1.00 56.73      A
```

FIGURE 25 CON'T

```
ATOM   5099  CG  TYR A 670      -7.970  31.781  27.187  1.00 56.73      A
ATOM   5100  CD1 TYR A 670      -8.536  32.992  27.584  1.00 56.73      A
ATOM   5101  CE1 TYR A 670      -8.507  34.109  26.742  1.00 56.73      A
ATOM   5102  CD2 TYR A 670      -7.381  31.711  25.922  1.00 56.73      A
ATOM   5103  CE2 TYR A 670      -7.349  32.812  25.082  1.00 56.73      A
ATOM   5104  CZ  TYR A 670      -7.911  34.005  25.496  1.00 56.73      A
ATOM   5105  OH  TYR A 670      -7.871  35.093  24.661  1.00 56.73      A
ATOM   5106  C   TYR A 670     -10.482  30.566  28.315  1.00 45.94      A
ATOM   5107  O   TYR A 670     -11.115  30.978  27.345  1.00 45.94      A
ATOM   5108  N   PHE A 671     -10.861  30.802  29.565  1.00 46.51      A
ATOM   5109  CA  PHE A 671     -12.061  31.576  29.847  1.00 46.51      A
ATOM   5110  CB  PHE A 671     -13.313  30.685  29.689  1.00 39.62      A
ATOM   5111  CG  PHE A 671     -13.316  29.452  30.570  1.00 39.62      A
ATOM   5112  CD1 PHE A 671     -13.831  29.495  31.860  1.00 39.62      A
ATOM   5113  CD2 PHE A 671     -12.805  28.246  30.102  1.00 39.62      A
ATOM   5114  CE1 PHE A 671     -13.838  28.340  32.680  1.00 39.62      A
ATOM   5115  CE2 PHE A 671     -12.807  27.089  30.910  1.00 39.62      A
ATOM   5116  CZ  PHE A 671     -13.325  27.143  32.201  1.00 39.62      A
ATOM   5117  C   PHE A 671     -12.011  32.167  31.247  1.00 46.51      A
ATOM   5118  O   PHE A 671     -11.259  31.696  32.105  1.00 46.51      A
ATOM   5119  N   ASN A 672     -12.815  33.200  31.473  1.00 46.97      A
ATOM   5120  CA  ASN A 672     -12.867  33.854  32.771  1.00 46.97      A
ATOM   5121  CB  ASN A 672     -13.041  35.373  32.607  1.00 66.45      A
ATOM   5122  CG  ASN A 672     -13.073  36.119  33.946  1.00 66.45      A
ATOM   5123  OD1 ASN A 672     -13.911  35.847  34.816  1.00 66.45      A
ATOM   5124  ND2 ASN A 672     -12.163  37.073  34.109  1.00 66.45      A
ATOM   5125  C   ASN A 672     -14.048  33.294  33.531  1.00 46.97      A
ATOM   5126  O   ASN A 672     -15.167  33.286  33.027  1.00 46.97      A
ATOM   5127  N   LEU A 673     -13.795  32.803  34.736  1.00 44.10      A
ATOM   5128  CA  LEU A 673     -14.862  32.272  35.560  1.00 44.10      A
ATOM   5129  CB  LEU A 673     -14.924  30.743  35.500  1.00 33.68      A
ATOM   5130  CG  LEU A 673     -15.806  30.104  36.581  1.00 33.68      A
ATOM   5131  CD1 LEU A 673     -17.270  30.492  36.333  1.00 33.68      A
ATOM   5132  CD2 LEU A 673     -15.648  28.595  36.564  1.00 33.68      A
ATOM   5133  C   LEU A 673     -14.591  32.700  36.971  1.00 44.10      A
ATOM   5134  O   LEU A 673     -13.539  32.393  37.526  1.00 44.10      A
ATOM   5135  N   GLY A 674     -15.541  33.426  37.542  1.00 48.61      A
ATOM   5136  CA  GLY A 674     -15.401  33.878  38.908  1.00 48.61      A
ATOM   5137  C   GLY A 674     -14.193  34.749  39.193  1.00 48.61      A
ATOM   5138  O   GLY A 674     -13.755  34.805  40.332  1.00 48.61      A
ATOM   5139  N   GLY A 675     -13.656  35.425  38.184  1.00 53.58      A
ATOM   5140  CA  GLY A 675     -12.504  36.278  38.418  1.00 53.58      A
ATOM   5141  C   GLY A 675     -11.166  35.615  38.151  1.00 53.58      A
ATOM   5142  O   GLY A 675     -10.120  36.262  38.192  1.00 53.58      A
ATOM   5143  N   ALA A 676     -11.189  34.317  37.876  1.00 53.60      A
ATOM   5144  CA  ALA A 676      -9.966  33.593  37.596  1.00 53.60      A
ATOM   5145  CB  ALA A 676      -9.863  32.373  38.511  1.00 39.76      A
ATOM   5146  C   ALA A 676      -9.999  33.161  36.144  1.00 53.60      A
ATOM   5147  O   ALA A 676     -11.070  33.063  35.554  1.00 53.60      A

ATOM   5148  N   ILE A 677      -8.832  32.920  35.558  1.00 48.00      A
ATOM   5149  CA  ILE A 677      -8.773  32.472  34.171  1.00 48.00      A
ATOM   5150  CB  ILE A 677      -7.716  33.245  33.350  1.00 51.13      A
ATOM   5151  CG2 ILE A 677      -7.626  32.656  31.945  1.00 51.13      A
ATOM   5152  CG1 ILE A 677      -8.047  34.741  33.326  1.00 51.13      A
ATOM   5153  CD1 ILE A 677      -9.436  35.080  32.826  1.00 51.13      A
ATOM   5154  C   ILE A 677      -8.399  30.998  34.133  1.00 48.00      A
```

FIGURE 25 CON'T

ATOM	5155	O	ILE	A	677	-7.429	30.582	34.771	1.00	48.00	A
ATOM	5156	N	TYR	A	678	-9.171	30.213	33.387	1.00	41.30	A
ATOM	5157	CA	TYR	A	678	-8.911	28.784	33.255	1.00	41.30	A
ATOM	5158	CB	TYR	A	678	-10.199	27.978	33.438	1.00	34.81	A
ATOM	5159	CG	TYR	A	678	-10.693	28.031	34.857	1.00	34.81	A
ATOM	5160	CD1	TYR	A	678	-10.378	27.016	35.770	1.00	34.81	A
ATOM	5161	CE1	TYR	A	678	-10.771	27.101	37.098	1.00	34.81	A
ATOM	5162	CD2	TYR	A	678	-11.419	29.128	35.315	1.00	34.81	A
ATOM	5163	CE2	TYR	A	678	-11.823	29.218	36.642	1.00	34.81	A
ATOM	5164	CZ	TYR	A	678	-11.497	28.205	37.522	1.00	34.81	A
ATOM	5165	OH	TYR	A	678	-11.930	28.288	38.820	1.00	34.81	A
ATOM	5166	C	TYR	A	678	-8.357	28.566	31.874	1.00	41.30	A
ATOM	5167	O	TYR	A	678	-8.950	29.006	30.894	1.00	41.30	A
ATOM	5168	N	LEU	A	679	-7.221	27.884	31.803	1.00	40.92	A
ATOM	5169	CA	LEU	A	679	-6.557	27.637	30.539	1.00	40.92	A
ATOM	5170	CB	LEU	A	679	-5.256	28.450	30.488	1.00	36.79	A
ATOM	5171	CG	LEU	A	679	-4.188	27.964	29.508	1.00	36.79	A
ATOM	5172	CD1	LEU	A	679	-4.568	28.325	28.063	1.00	36.79	A
ATOM	5173	CD2	LEU	A	679	-2.866	28.601	29.883	1.00	36.79	A
ATOM	5174	C	LEU	A	679	-6.239	26.171	30.279	1.00	40.92	A
ATOM	5175	O	LEU	A	679	-5.623	25.505	31.114	1.00	40.92	A
ATOM	5176	N	ILE	A	680	-6.671	25.674	29.124	1.00	44.94	A
ATOM	5177	CA	ILE	A	680	-6.381	24.307	28.712	1.00	44.94	A
ATOM	5178	CB	ILE	A	680	-7.613	23.603	28.079	1.00	45.17	A
ATOM	5179	CG2	ILE	A	680	-7.185	22.297	27.409	1.00	45.17	A
ATOM	5180	CG1	ILE	A	680	-8.664	23.276	29.151	1.00	45.17	A
ATOM	5181	CD1	ILE	A	680	-9.443	24.462	29.677	1.00	45.17	A
ATOM	5182	C	ILE	A	680	-5.275	24.501	27.662	1.00	44.94	A
ATOM	5183	O	ILE	A	680	-5.535	24.935	26.537	1.00	44.94	A
ATOM	5184	N	PRO	A	681	-4.015	24.213	28.038	1.00	59.08	A
ATOM	5185	CD	PRO	A	681	-3.637	23.794	29.398	1.00	62.16	A
ATOM	5186	CA	PRO	A	681	-2.819	24.341	27.195	1.00	59.08	A
ATOM	5187	CB	PRO	A	681	-1.681	23.971	28.149	1.00	62.16	A
ATOM	5188	CG	PRO	A	681	-2.225	24.303	29.490	1.00	62.16	A
ATOM	5189	C	PRO	A	681	-2.795	23.479	25.939	1.00	59.08	A
ATOM	5190	O	PRO	A	681	-2.228	23.868	24.916	1.00	59.08	A
ATOM	5191	N	HIS	A	682	-3.388	22.297	26.029	1.00	56.26	A
ATOM	5192	CA	HIS	A	682	-3.417	21.384	24.895	1.00	56.26	A
ATOM	5193	CB	HIS	A	682	-2.070	20.667	24.776	1.00	89.86	A
ATOM	5194	CG	HIS	A	682	-1.447	20.337	26.098	1.00	89.86	A
ATOM	5195	CD2	HIS	A	682	-0.291	20.755	26.668	1.00	89.86	A
ATOM	5196	ND1	HIS	A	682	-2.044	19.499	27.014	1.00	89.86	A
ATOM	5197	CE1	HIS	A	682	-1.284	19.415	28.092	1.00	89.86	A
ATOM	5198	NE2	HIS	A	682	-0.214	20.168	27.907	1.00	89.86	A
ATOM	5199	C	HIS	A	682	-4.537	20.374	25.055	1.00	56.26	A
ATOM	5200	O	HIS	A	682	-5.056	20.181	26.155	1.00	56.26	A
ATOM	5201	N	LYS	A	683	-4.912	19.734	23.954	1.00	68.26	A
ATOM	5202	CA	LYS	A	683	-5.970	18.735	23.984	1.00	68.26	A
ATOM	5203	CB	LYS	A	683	-6.773	18.774	22.683	1.00	76.15	A
ATOM	5204	CG	LYS	A	683	-5.963	18.410	21.448	1.00	76.15	A
ATOM	5205	CD	LYS	A	683	-6.791	18.519	20.173	1.00	76.15	A
ATOM	5206	CE	LYS	A	683	-7.935	17.519	20.155	1.00	76.15	A
ATOM	5207	NZ	LYS	A	683	-8.770	17.654	18.928	1.00	76.15	A
ATOM	5208	C	LYS	A	683	-5.332	17.365	24.148	1.00	68.26	A
ATOM	5209	O	LYS	A	683	-4.148	17.197	23.868	1.00	68.26	A
ATOM	5210	N	LEU	A	684	-6.110	16.394	24.612	1.00	72.49	A
ATOM	5211	CA	LEU	A	684	-5.605	15.037	24.782	1.00	72.49	A

FIGURE 25 CON'T

ATOM	5212	CB	LEU	A	684	-6.517	14.249	25.726	1.00	77.72	A
ATOM	5213	CG	LEU	A	684	-6.837	14.940	27.058	1.00	77.72	A
ATOM	5214	CD1	LEU	A	684	-7.772	14.064	27.872	1.00	77.72	A
ATOM	5215	CD2	LEU	A	684	-5.551	15.220	27.828	1.00	77.72	A
ATOM	5216	C	LEU	A	684	-5.589	14.397	23.392	1.00	72.49	A
ATOM	5217	O	LEU	A	684	-6.638	14.185	22.783	1.00	72.49	A
ATOM	5218	N	LYS	A	685	-4.396	14.094	22.894	1.00	133.17	A
ATOM	5219	CA	LYS	A	685	-4.249	13.521	21.561	1.00	133.17	A
ATOM	5220	CB	LYS	A	685	-2.963	14.055	20.925	1.00	83.35	A
ATOM	5221	CG	LYS	A	685	-2.918	15.575	20.877	1.00	83.35	A
ATOM	5222	CD	LYS	A	685	-1.585	16.102	20.376	1.00	83.35	A
ATOM	5223	CE	LYS	A	685	-1.552	17.624	20.435	1.00	83.35	A
ATOM	5224	NZ	LYS	A	685	-0.230	18.177	20.033	1.00	83.35	A
ATOM	5225	C	LYS	A	685	-4.264	11.997	21.500	1.00	133.17	A
ATOM	5226	O	LYS	A	685	-4.633	11.417	20.478	1.00	133.17	A
ATOM	5227	N	GLN	A	686	-3.874	11.348	22.590	1.00	127.17	A
ATOM	5228	CA	GLN	A	686	-3.840	9.891	22.621	1.00	127.17	A
ATOM	5229	CB	GLN	A	686	-2.389	9.415	22.755	1.00	115.22	A
ATOM	5230	CG	GLN	A	686	-2.193	7.913	22.616	1.00	115.22	A
ATOM	5231	CD	GLN	A	686	-0.734	7.503	22.725	1.00	115.22	A
ATOM	5232	OE1	GLN	A	686	-0.112	7.651	23.778	1.00	115.22	A
ATOM	5233	NE2	GLN	A	686	-0.180	6.991	21.632	1.00	115.22	A
ATOM	5234	C	GLN	A	686	-4.673	9.327	23.765	1.00	127.17	A
ATOM	5235	O	GLN	A	686	-5.658	8.620	23.547	1.00	127.17	A
ATOM	5236	N	ALA	A	687	-4.270	9.660	24.986	1.00	137.90	A
ATOM	5237	CA	ALA	A	687	-4.940	9.182	26.188	1.00	137.90	A
ATOM	5238	CB	ALA	A	687	-4.156	9.627	27.417	1.00	80.16	A
ATOM	5239	C	ALA	A	687	-6.405	9.590	26.332	1.00	137.90	A
ATOM	5240	O	ALA	A	687	-6.863	10.573	25.746	1.00	137.90	A
ATOM	5241	N	LYS	A	688	-7.120	8.804	27.130	1.00	71.04	A
ATOM	5242	CA	LYS	A	688	-8.535	9.002	27.435	1.00	71.04	A
ATOM	5243	CB	LYS	A	688	-9.141	7.650	27.840	1.00	77.29	A
ATOM	5244	CG	LYS	A	688	-10.629	7.631	28.170	1.00	77.29	A
ATOM	5245	CD	LYS	A	688	-11.058	6.193	28.479	1.00	77.29	A
ATOM	5246	CE	LYS	A	688	-12.575	6.019	28.587	1.00	77.29	A
ATOM	5247	NZ	LYS	A	688	-13.181	6.589	29.824	1.00	77.29	A
ATOM	5248	C	LYS	A	688	-8.641	10.002	28.595	1.00	71.04	A
ATOM	5249	O	LYS	A	688	-7.681	10.198	29.342	1.00	71.04	A
ATOM	5250	N	GLY	A	689	-9.797	10.643	28.738	1.00	50.26	A
ATOM	5251	CA	GLY	A	689	-9.965	11.587	29.831	1.00	50.26	A
ATOM	5252	C	GLY	A	689	-10.447	12.966	29.425	1.00	50.26	A
ATOM	5253	O	GLY	A	689	-10.707	13.221	28.251	1.00	50.26	A
ATOM	5254	N	THR	A	690	-10.558	13.852	30.413	1.00	41.72	A
ATOM	5255	CA	THR	A	690	-11.010	15.221	30.205	1.00	41.72	A
ATOM	5256	CB	THR	A	690	-12.225	15.532	31.104	1.00	44.55	A
ATOM	5257	OG1	THR	A	690	-13.314	14.669	30.753	1.00	44.55	A
ATOM	5258	CG2	THR	A	690	-12.665	16.976	30.941	1.00	44.55	A
ATOM	5259	C	THR	A	690	-9.854	16.155	30.558	1.00	41.72	A
ATOM	5260	O	THR	A	690	-9.222	16.003	31.599	1.00	41.72	A
ATOM	5261	N	PRO	A	691	-9.561	17.136	29.692	1.00	42.74	A
ATOM	5262	CD	PRO	A	691	-10.298	17.505	28.471	1.00	43.40	A
ATOM	5263	CA	PRO	A	691	-8.460	18.076	29.946	1.00	42.74	A
ATOM	5264	CB	PRO	A	691	-8.571	19.076	28.794	1.00	43.40	A
ATOM	5265	CG	PRO	A	691	-9.256	18.299	27.710	1.00	43.40	A
ATOM	5266	C	PRO	A	691	-8.573	18.776	31.298	1.00	42.74	A
ATOM	5267	O	PRO	A	691	-9.661	19.157	31.731	1.00	42.74	A
ATOM	5268	N	ILE	A	692	-7.441	18.945	31.965	1.00	47.28	A

FIGURE 25 CON'T

```
ATOM   5269  CA  ILE A 692      -7.435  19.616  33.245  1.00 47.28      A
ATOM   5270  CB  ILE A 692      -6.587  18.874  34.265  1.00 42.24      A
ATOM   5271  CG2 ILE A 692      -6.732  19.556  35.624  1.00 42.24      A
ATOM   5272  CG1 ILE A 692      -7.028  17.402  34.315  1.00 42.24      A
ATOM   5273  CD1 ILE A 692      -6.274  16.553  35.343  1.00 42.24      A
ATOM   5274  C   ILE A 692      -6.878  21.010  33.051  1.00 47.28      A
ATOM   5275  O   ILE A 692      -5.707  21.180  32.746  1.00 47.28      A

ATOM   5276  N   PRO A 693      -7.725  22.032  33.224  1.00 45.32      A
ATOM   5277  CD  PRO A 693      -9.147  21.972  33.594  1.00 36.54      A
ATOM   5278  CA  PRO A 693      -7.287  23.416  33.055  1.00 45.32      A
ATOM   5279  CB  PRO A 693      -8.592  24.223  33.135  1.00 36.54      A
ATOM   5280  CG  PRO A 693      -9.690  23.205  32.926  1.00 36.54      A
ATOM   5281  C   PRO A 693      -6.334  23.861  34.147  1.00 45.32      A
ATOM   5282  O   PRO A 693      -6.356  23.340  35.260  1.00 45.32      A
ATOM   5283  N   ILE A 694      -5.504  24.840  33.819  1.00 38.05      A
ATOM   5284  CA  ILE A 694      -4.620  25.424  34.802  1.00 38.05      A
ATOM   5285  CB  ILE A 694      -3.313  25.934  34.178  1.00 57.89      A
ATOM   5286  CG2 ILE A 694      -2.505  26.688  35.220  1.00 57.89      A
ATOM   5287  CG1 ILE A 694      -2.511  24.769  33.616  1.00 57.89      A
ATOM   5288  CD1 ILE A 694      -1.279  25.216  32.844  1.00 57.89      A
ATOM   5289  C   ILE A 694      -5.423  26.641  35.232  1.00 38.05      A
ATOM   5290  O   ILE A 694      -5.916  27.378  34.378  1.00 38.05      A
ATOM   5291  N   LYS A 695      -5.551  26.864  36.535  1.00 40.66      A
ATOM   5292  CA  LYS A 695      -6.286  28.010  37.034  1.00 40.66      A
ATOM   5293  CB  LYS A 695      -7.098  27.591  38.256  1.00 39.88      A
ATOM   5294  CG  LYS A 695      -7.929  28.690  38.877  1.00 39.88      A
ATOM   5295  CD  LYS A 695      -8.674  28.164  40.097  1.00 39.88      A
ATOM   5296  CE  LYS A 695      -9.491  29.258  40.772  1.00 39.88      A
ATOM   5297  NZ  LYS A 695     -10.134  28.753  42.038  1.00 39.88      A
ATOM   5298  C   LYS A 695      -5.317  29.155  37.392  1.00 40.66      A
ATOM   5299  O   LYS A 695      -4.383  28.978  38.188  1.00 40.66      A
ATOM   5300  N   LEU A 696      -5.537  30.325  36.793  1.00 47.41      A
ATOM   5301  CA  LEU A 696      -4.693  31.492  37.032  1.00 47.41      A
ATOM   5302  CB  LEU A 696      -4.206  32.072  35.705  1.00 40.52      A
ATOM   5303  CG  LEU A 696      -3.545  31.121  34.723  1.00 40.52      A
ATOM   5304  CD1 LEU A 696      -3.303  31.831  33.394  1.00 40.52      A
ATOM   5305  CD2 LEU A 696      -2.245  30.620  35.321  1.00 40.52      A
ATOM   5306  C   LEU A 696      -5.500  32.549  37.766  1.00 47.41      A
ATOM   5307  O   LEU A 696      -6.610  32.872  37.344  1.00 47.41      A
ATOM   5308  N   ALA A 697      -4.955  33.091  38.858  1.00 44.29      A
ATOM   5309  CA  ALA A 697      -5.683  34.109  39.616  1.00 44.29      A
ATOM   5310  CB  ALA A 697      -6.798  33.446  40.404  1.00 65.48      A
ATOM   5311  C   ALA A 697      -4.845  34.989  40.557  1.00 44.29      A
ATOM   5312  O   ALA A 697      -3.669  34.710  40.827  1.00 44.29      A
ATOM   5313  N   LYS A 698      -5.481  36.053  41.051  1.00 43.91      A
ATOM   5314  CA  LYS A 698      -4.869  36.994  41.982  1.00 43.91      A
ATOM   5315  CB  LYS A 698      -4.782  36.372  43.379  1.00 72.05      A
ATOM   5316  CG  LYS A 698      -6.125  35.997  43.975  1.00 72.05      A
ATOM   5317  CD  LYS A 698      -5.951  35.321  45.324  1.00 72.05      A
ATOM   5318  CE  LYS A 698      -7.290  34.913  45.917  1.00 72.05      A
ATOM   5319  NZ  LYS A 698      -7.120  34.130  47.182  1.00 72.05      A
ATOM   5320  C   LYS A 698      -3.489  37.459  41.553  1.00 43.91      A
ATOM   5321  O   LYS A 698      -2.544  37.414  42.331  1.00 43.91      A
ATOM   5322  N   LYS A 699      -3.373  37.899  40.309  1.00 59.17      A
ATOM   5323  CA  LYS A 699      -2.109  38.386  39.801  1.00 59.17      A
ATOM   5324  CB  LYS A 699      -2.236  38.668  38.308  1.00 58.69      A
```

FIGURE 25 CON'T

ATOM	5325	CG	LYS	A	699	-0.983	39.210	37.659	1.00	58.69	A
ATOM	5326	CD	LYS	A	699	-1.126	39.200	36.145	1.00	58.69	A
ATOM	5327	CE	LYS	A	699	0.087	39.802	35.475	1.00	58.69	A
ATOM	5328	NZ	LYS	A	699	0.275	41.205	35.928	1.00	58.69	A
ATOM	5329	C	LYS	A	699	-1.788	39.666	40.559	1.00	59.17	A
ATOM	5330	O	LYS	A	699	-2.690	40.337	41.058	1.00	59.17	A
ATOM	5331	N	ARG	A	700	-0.509	39.997	40.675	1.00	53.00	A
ATOM	5332	CA	ARG	A	700	-0.119	41.212	41.375	1.00	53.00	A
ATOM	5333	CB	ARG	A	700	-0.174	40.998	42.884	1.00	71.74	A
ATOM	5334	CG	ARG	A	700	0.951	40.143	43.410	1.00	71.74	A
ATOM	5335	CD	ARG	A	700	0.809	39.858	44.896	1.00	71.74	A
ATOM	5336	NE	ARG	A	700	-0.252	38.902	45.223	1.00	71.74	A
ATOM	5337	CZ	ARG	A	700	-0.420	37.724	44.629	1.00	71.74	A
ATOM	5338	NH1	ARG	A	700	0.394	37.343	43.655	1.00	71.74	A
ATOM	5339	NH2	ARG	A	700	-1.380	36.904	45.032	1.00	71.74	A
ATOM	5340	C	ARG	A	700	1.286	41.619	40.958	1.00	53.00	A
ATOM	5341	O	ARG	A	700	2.062	40.798	40.463	1.00	53.00	A
ATOM	5342	N	ILE	A	701	1.605	42.896	41.142	1.00	59.98	A
ATOM	5343	CA	ILE	A	701	2.925	43.417	40.797	1.00	59.98	A
ATOM	5344	CB	ILE	A	701	2.824	44.566	39.780	1.00	73.76	A
ATOM	5345	CG2	ILE	A	701	1.938	45.668	40.332	1.00	73.76	A
ATOM	5346	CG1	ILE	A	701	4.213	45.131	39.485	1.00	73.76	A
ATOM	5347	CD1	ILE	A	701	5.133	44.162	38.812	1.00	73.76	A
ATOM	5348	C	ILE	A	701	3.563	43.948	42.071	1.00	59.98	A
ATOM	5349	O	ILE	A	701	2.904	44.593	42.881	1.00	59.98	A
ATOM	5350	N	ILE	A	702	4.844	43.670	42.258	1.00	61.88	A
ATOM	5351	CA	ILE	A	702	5.521	44.139	43.452	1.00	61.88	A
ATOM	5352	CB	ILE	A	702	5.989	42.956	44.330	1.00	70.36	A
ATOM	5353	CG2	ILE	A	702	6.488	43.471	45.676	1.00	70.36	A
ATOM	5354	CG1	ILE	A	702	4.822	41.989	44.558	1.00	70.36	A
ATOM	5355	CD1	ILE	A	702	5.168	40.803	45.437	1.00	70.36	A
ATOM	5356	C	ILE	A	702	6.714	45.001	43.073	1.00	61.88	A
ATOM	5357	O	ILE	A	702	7.685	44.511	42.501	1.00	61.88	A
ATOM	5358	N	LYS	A	703	6.617	46.291	43.387	1.00	76.24	A
ATOM	5359	CA	LYS	A	703	7.673	47.257	43.094	1.00	76.24	A
ATOM	5360	CB	LYS	A	703	7.181	48.332	42.122	1.00	89.04	A
ATOM	5361	CG	LYS	A	703	6.615	47.828	40.814	1.00	89.04	A
ATOM	5362	CD	LYS	A	703	6.088	48.998	39.991	1.00	89.04	A
ATOM	5363	CE	LYS	A	703	5.294	48.536	38.777	1.00	89.04	A
ATOM	5364	NZ	LYS	A	703	4.798	49.691	37.972	1.00	89.04	A
ATOM	5365	C	LYS	A	703	8.089	47.940	44.388	1.00	76.24	A
ATOM	5366	O	LYS	A	703	7.247	48.284	45.217	1.00	76.24	A
ATOM	5367	N	ASN	A	704	9.391	48.137	44.552	1.00	76.83	A
ATOM	5368	CA	ASN	A	704	9.920	48.797	45.735	1.00	76.83	A
ATOM	5369	CB	ASN	A	704	9.793	50.312	45.573	1.00	83.90	A
ATOM	5370	CG	ASN	A	704	10.302	50.794	44.229	1.00	83.90	A
ATOM	5371	OD1	ASN	A	704	11.483	50.642	43.905	1.00	83.90	A
ATOM	5372	ND2	ASN	A	704	9.409	51.369	43.433	1.00	83.90	A
ATOM	5373	C	ASN	A	704	9.218	48.351	47.015	1.00	76.83	A
ATOM	5374	O	ASN	A	704	8.875	49.173	47.868	1.00	76.83	A
ATOM	5375	N	GLY	A	705	8.987	47.046	47.132	1.00	60.58	A
ATOM	5376	CA	GLY	A	705	8.357	46.504	48.324	1.00	60.58	A
ATOM	5377	C	GLY	A	705	6.867	46.724	48.461	1.00	60.58	A
ATOM	5378	O	GLY	A	705	6.284	46.380	49.492	1.00	60.58	A
ATOM	5379	N	LYS	A	706	6.241	47.285	47.434	1.00	69.84	A
ATOM	5380	CA	LYS	A	706	4.805	47.533	47.479	1.00	69.84	A
ATOM	5381	CB	LYS	A	706	4.514	49.008	47.190	1.00	118.05	A

FIGURE 25 CON'T

```
ATOM   5382  CG  LYS A 706       4.906  49.937  48.328  1.00118.05      A
ATOM   5383  CD  LYS A 706       4.159  49.575  49.605  1.00118.05      A
ATOM   5384  CE  LYS A 706       4.587  50.451  50.771  1.00118.05      A
ATOM   5385  NZ  LYS A 706       3.854  50.103  52.022  1.00118.05      A
ATOM   5386  C   LYS A 706       4.011  46.644  46.525  1.00 69.84      A
ATOM   5387  O   LYS A 706       4.396  46.444  45.368  1.00 69.84      A
ATOM   5388  N   VAL A 707       2.891  46.126  47.028  1.00 58.45      A
ATOM   5389  CA  VAL A 707       2.021  45.242  46.262  1.00 58.45      A
ATOM   5390  CB  VAL A 707       1.510  44.085  47.139  1.00 55.42      A
ATOM   5391  CG1 VAL A 707       0.611  43.165  46.316  1.00 55.42      A
ATOM   5392  CG2 VAL A 707       2.686  43.322  47.713  1.00 55.42      A
ATOM   5393  C   VAL A 707       0.806  45.942  45.654  1.00 58.45      A
ATOM   5394  O   VAL A 707       0.056  46.638  46.341  1.00 58.45      A
ATOM   5395  N   GLU A 708       0.613  45.728  44.358  1.00 65.11      A
ATOM   5396  CA  GLU A 708      -0.505  46.314  43.638  1.00 65.11      A
ATOM   5397  CB  GLU A 708       0.009  47.375  42.662  1.00156.55      A
ATOM   5398  CG  GLU A 708       0.849  48.454  43.329  1.00156.55      A
ATOM   5399  CD  GLU A 708       1.445  49.432  42.337  1.00156.55      A
ATOM   5400  OE1 GLU A 708       2.219  48.992  41.461  1.00156.55      A
ATOM   5401  OE2 GLU A 708       1.142  50.639  42.437  1.00156.55      A
ATOM   5402  C   GLU A 708      -1.254  45.221  42.879  1.00 65.11      A
ATOM   5403  O   GLU A 708      -0.801  44.759  41.831  1.00 65.11      A

ATOM   5404  N   LYS A 709      -2.396  44.805  43.419  1.00 65.35      A
ATOM   5405  CA  LYS A 709      -3.209  43.768  42.789  1.00 65.35      A
ATOM   5406  CB  LYS A 709      -4.548  43.622  43.511  1.00 70.74      A
ATOM   5407  CG  LYS A 709      -4.436  43.305  44.994  1.00 70.74      A
ATOM   5408  CD  LYS A 709      -5.814  43.089  45.594  1.00 70.74      A
ATOM   5409  CE  LYS A 709      -5.747  42.919  47.099  1.00 70.74      A
ATOM   5410  NZ  LYS A 709      -7.099  42.643  47.674  1.00 70.74      A
ATOM   5411  C   LYS A 709      -3.459  44.150  41.342  1.00 65.35      A
ATOM   5412  O   LYS A 709      -3.913  45.256  41.063  1.00 65.35      A
ATOM   5413  N   GLN A 710      -3.158  43.240  40.422  1.00 72.53      A
ATOM   5414  CA  GLN A 710      -3.349  43.518  39.006  1.00 72.53      A
ATOM   5415  CB  GLN A 710      -2.044  43.291  38.239  1.00112.53      A
ATOM   5416  CG  GLN A 710      -1.769  44.344  37.178  1.00112.53      A
ATOM   5417  CD  GLN A 710      -1.363  45.681  37.779  1.00112.53      A
ATOM   5418  OE1 GLN A 710      -0.239  45.845  38.252  1.00112.53      A
ATOM   5419  NE2 GLN A 710      -2.281  46.641  37.770  1.00112.53      A
ATOM   5420  C   GLN A 710      -4.445  42.635  38.421  1.00 72.53      A
ATOM   5421  O   GLN A 710      -5.155  41.940  39.153  1.00 72.53      A
ATOM   5422  N   SER A 711      -4.583  42.676  37.100  1.00 67.00      A
ATOM   5423  CA  SER A 711      -5.580  41.879  36.407  1.00 67.00      A
ATOM   5424  CB  SER A 711      -6.606  42.787  35.725  1.00106.90      A
ATOM   5425  OG  SER A 711      -7.311  43.564  36.677  1.00106.90      A
ATOM   5426  C   SER A 711      -4.870  41.025  35.369  1.00 67.00      A
ATOM   5427  O   SER A 711      -3.918  41.481  34.737  1.00 67.00      A
ATOM   5428  N   ILE A 712      -5.327  39.787  35.203  1.00 59.42      A
ATOM   5429  CA  ILE A 712      -4.720  38.876  34.244  1.00 59.42      A
ATOM   5430  CB  ILE A 712      -5.131  37.410  34.543  1.00 44.31      A
ATOM   5431  CG2 ILE A 712      -4.562  36.465  33.476  1.00 44.31      A
ATOM   5432  CG1 ILE A 712      -4.627  37.019  35.939  1.00 44.31      A
ATOM   5433  CD1 ILE A 712      -5.076  35.659  36.406  1.00 44.31      A
ATOM   5434  C   ILE A 712      -5.164  39.291  32.846  1.00 59.42      A
ATOM   5435  O   ILE A 712      -6.334  39.621  32.636  1.00 59.42      A
ATOM   5436  N   THR A 713      -4.220  39.278  31.905  1.00 58.31      A
ATOM   5437  CA  THR A 713      -4.469  39.685  30.527  1.00 58.31      A
```

FIGURE 25 CON'T

```
ATOM   5438  CB  THR A 713      -3.509  40.806  30.107  1.00 60.66      A
ATOM   5439  OG1 THR A 713      -2.184  40.266  29.989  1.00 60.66      A
ATOM   5440  CG2 THR A 713      -3.501  41.922  31.140  1.00 60.66      A
ATOM   5441  C   THR A 713      -4.275  38.545  29.541  1.00 58.31      A
ATOM   5442  O   THR A 713      -3.750  37.484  29.883  1.00 58.31      A
ATOM   5443  N   ARG A 714      -4.690  38.774  28.304  1.00 56.92      A
ATOM   5444  CA  ARG A 714      -4.542  37.759  27.281  1.00 56.92      A
ATOM   5445  CB  ARG A 714      -5.152  38.236  25.963  1.00101.08      A
ATOM   5446  CG  ARG A 714      -6.647  38.453  26.038  1.00101.08      A
ATOM   5447  CD  ARG A 714      -7.249  38.679  24.667  1.00101.08      A
ATOM   5448  NE  ARG A 714      -8.703  38.774  24.735  1.00101.08      A
ATOM   5449  CZ  ARG A 714      -9.498  38.851  23.674  1.00101.08      A
ATOM   5450  NH1 ARG A 714      -8.982  38.844  22.451  1.00101.08      A
ATOM   5451  NH2 ARG A 714     -10.812  38.929  23.837  1.00101.08      A
ATOM   5452  C   ARG A 714      -3.060  37.457  27.099  1.00 56.92      A
ATOM   5453  O   ARG A 714      -2.677  36.314  26.847  1.00 56.92      A
ATOM   5454  N   GLN A 715      -2.231  38.489  27.227  1.00 57.29      A
ATOM   5455  CA  GLN A 715      -0.787  38.331  27.092  1.00 57.29      A
ATOM   5456  CB  GLN A 715      -0.086  39.689  27.192  1.00 91.22      A
ATOM   5457  CG  GLN A 715       0.676  40.091  25.933  1.00 91.22      A
ATOM   5458  CD  GLN A 715       1.793  39.121  25.584  1.00 91.22      A
ATOM   5459  OE1 GLN A 715       2.695  38.886  26.385  1.00 91.22      A
ATOM   5460  NE2 GLN A 715       1.739  38.559  24.382  1.00 91.22      A
ATOM   5461  C   GLN A 715      -0.262  37.397  28.184  1.00 57.29      A
ATOM   5462  O   GLN A 715       0.594  36.554  27.925  1.00 57.29      A
ATOM   5463  N   ASP A 716      -0.779  37.558  29.397  1.00 55.13      A
ATOM   5464  CA  ASP A 716      -0.382  36.714  30.522  1.00 55.13      A
ATOM   5465  CB  ASP A 716      -1.094  37.150  31.805  1.00 51.94      A
ATOM   5466  CG  ASP A 716      -0.634  38.507  32.297  1.00 51.94      A
ATOM   5467  OD1 ASP A 716       0.550  38.848  32.095  1.00 51.94      A
ATOM   5468  OD2 ASP A 716      -1.455  39.232  32.903  1.00 51.94      A
ATOM   5469  C   ASP A 716      -0.717  35.254  30.234  1.00 55.13      A
ATOM   5470  O   ASP A 716       0.080  34.354  30.518  1.00 55.13      A
ATOM   5471  N   VAL A 717      -1.899  35.028  29.664  1.00 45.86      A
ATOM   5472  CA  VAL A 717      -2.344  33.682  29.332  1.00 45.86      A
ATOM   5473  CB  VAL A 717      -3.820  33.686  28.836  1.00 41.48      A
ATOM   5474  CG1 VAL A 717      -4.220  32.289  28.340  1.00 41.48      A
ATOM   5475  CG2 VAL A 717      -4.749  34.154  29.965  1.00 41.48      A
ATOM   5476  C   VAL A 717      -1.435  33.119  28.249  1.00 45.86      A
ATOM   5477  O   VAL A 717      -1.135  31.918  28.228  1.00 45.86      A
ATOM   5478  N   LEU A 718      -0.992  33.989  27.350  1.00 48.09      A
ATOM   5479  CA  LEU A 718      -0.096  33.575  26.267  1.00 48.09      A
ATOM   5480  CB  LEU A 718       0.150  34.740  25.300  1.00 64.92      A
ATOM   5481  CG  LEU A 718       0.401  34.446  23.815  1.00 64.92      A
ATOM   5482  CD1 LEU A 718       0.989  35.702  23.173  1.00 64.92      A
ATOM   5483  CD2 LEU A 718       1.349  33.281  23.625  1.00 64.92      A
ATOM   5484  C   LEU A 718       1.249  33.136  26.870  1.00 48.09      A
ATOM   5485  O   LEU A 718       1.821  32.127  26.459  1.00 48.09      A
ATOM   5486  N   ASP A 719       1.754  33.907  27.830  1.00 48.83      A
ATOM   5487  CA  ASP A 719       3.021  33.569  28.475  1.00 48.83      A
ATOM   5488  CB  ASP A 719       3.395  34.617  29.532  1.00 48.69      A
ATOM   5489  CG  ASP A 719       3.735  35.981  28.926  1.00 48.69      A
ATOM   5490  OD1 ASP A 719       4.239  36.028  27.779  1.00 48.69      A
ATOM   5491  OD2 ASP A 719       3.518  37.008  29.608  1.00 48.69      A
ATOM   5492  C   ASP A 719       2.907  32.187  29.134  1.00 48.83      A
ATOM   5493  O   ASP A 719       3.697  31.281  28.842  1.00 48.83      A
ATOM   5494  N   ILE A 720       1.916  32.024  30.012  1.00 43.40      A
```

FIGURE 25 CON'T

ATOM	5495	CA	ILE	A	720	1.713	30.746	30.686	1.00	43.40	A
ATOM	5496	CB	ILE	A	720	0.407	30.734	31.507	1.00	41.33	A
ATOM	5497	CG2	ILE	A	720	0.146	29.326	32.050	1.00	41.33	A
ATOM	5498	CG1	ILE	A	720	0.506	31.741	32.648	1.00	41.33	A
ATOM	5499	CD1	ILE	A	720	1.710	31.509	33.584	1.00	41.33	A
ATOM	5500	C	ILE	A	720	1.639	29.646	29.646	1.00	43.40	A
ATOM	5501	O	ILE	A	720	2.271	28.596	29.781	1.00	43.40	A
ATOM	5502	N	PHE	A	721	0.872	29.904	28.594	1.00	42.36	A
ATOM	5503	CA	PHE	A	721	0.717	28.938	27.518	1.00	42.36	A
ATOM	5504	CB	PHE	A	721	-0.127	29.518	26.382	1.00	49.57	A
ATOM	5505	CG	PHE	A	721	-0.237	28.604	25.199	1.00	49.57	A
ATOM	5506	CD1	PHE	A	721	-1.096	27.515	25.226	1.00	49.57	A
ATOM	5507	CD2	PHE	A	721	0.539	28.819	24.064	1.00	49.57	A
ATOM	5508	CE1	PHE	A	721	-1.186	26.649	24.134	1.00	49.57	A
ATOM	5509	CE2	PHE	A	721	0.458	27.963	22.973	1.00	49.57	A
ATOM	5510	CZ	PHE	A	721	-0.407	26.874	23.004	1.00	49.57	A
ATOM	5511	C	PHE	A	721	2.061	28.509	26.949	1.00	42.36	A
ATOM	5512	O	PHE	A	721	2.331	27.312	26.804	1.00	42.36	A
ATOM	5513	N	ILE	A	722	2.899	29.482	26.608	1.00	51.86	A
ATOM	5514	CA	ILE	A	722	4.203	29.162	26.041	1.00	51.86	A
ATOM	5515	CB	ILE	A	722	4.981	30.446	25.634	1.00	49.95	A
ATOM	5516	CG2	ILE	A	722	6.258	30.070	24.893	1.00	49.95	A
ATOM	5517	CG1	ILE	A	722	4.120	31.306	24.703	1.00	49.95	A
ATOM	5518	CD1	ILE	A	722	3.723	30.615	23.418	1.00	49.95	A
ATOM	5519	C	ILE	A	722	5.020	28.355	27.051	1.00	51.86	A
ATOM	5520	O	ILE	A	722	5.552	27.296	26.722	1.00	51.86	A
ATOM	5521	N	LEU	A	723	5.093	28.848	28.282	1.00	50.06	A
ATOM	5522	CA	LEU	A	723	5.837	28.174	29.341	1.00	50.06	A
ATOM	5523	CB	LEU	A	723	5.687	28.939	30.653	1.00	43.52	A
ATOM	5524	CG	LEU	A	723	6.300	30.340	30.634	1.00	43.52	A
ATOM	5525	CD1	LEU	A	723	6.051	31.040	31.970	1.00	43.52	A
ATOM	5526	CD2	LEU	A	723	7.802	30.226	30.347	1.00	43.52	A
ATOM	5527	C	LEU	A	723	5.383	26.736	29.535	1.00	50.06	A
ATOM	5528	O	LEU	A	723	6.153	25.883	29.982	1.00	50.06	A
ATOM	5529	N	THR	A	724	4.126	26.466	29.205	1.00	48.74	A
ATOM	5530	CA	THR	A	724	3.598	25.121	29.340	1.00	48.74	A
ATOM	5531	CB	THR	A	724	2.056	25.140	29.419	1.00	65.45	A
ATOM	5532	OG1	THR	A	724	1.655	25.818	30.616	1.00	65.45	A
ATOM	5533	CG2	THR	A	724	1.502	23.730	29.447	1.00	65.45	A
ATOM	5534	C	THR	A	724	4.036	24.226	28.188	1.00	48.74	A
ATOM	5535	O	THR	A	724	4.061	23.006	28.327	1.00	48.74	A
ATOM	5536	N	ARG	A	725	4.387	24.820	27.051	1.00	47.84	A
ATOM	5537	CA	ARG	A	725	4.815	24.021	25.903	1.00	47.84	A
ATOM	5538	CB	ARG	A	725	4.466	24.742	24.595	1.00	76.71	A
ATOM	5539	CG	ARG	A	725	2.969	24.777	24.302	1.00	76.71	A
ATOM	5540	CD	ARG	A	725	2.377	23.391	24.508	1.00	76.71	A
ATOM	5541	NE	ARG	A	725	0.969	23.300	24.145	1.00	76.71	A
ATOM	5542	CZ	ARG	A	725	0.525	23.274	22.895	1.00	76.71	A
ATOM	5543	NH1	ARG	A	725	1.382	23.335	21.883	1.00	76.71	A
ATOM	5544	NH2	ARG	A	725	-0.775	23.171	22.659	1.00	76.71	A
ATOM	5545	C	ARG	A	725	6.297	23.635	25.910	1.00	47.84	A
ATOM	5546	O	ARG	A	725	6.771	22.967	24.999	1.00	47.84	A
ATOM	5547	N	LEU	A	726	7.029	24.048	26.938	1.00	53.00	A
ATOM	5548	CA	LEU	A	726	8.444	23.702	27.031	1.00	53.00	A
ATOM	5549	CB	LEU	A	726	9.206	24.873	27.672	1.00	47.46	A
ATOM	5550	CG	LEU	A	726	9.077	26.189	26.878	1.00	47.46	A

FIGURE 25 CON'T

ATOM	5551	CD1	LEU	A	726	9.639	27.362	27.667	1.00	47.46	A
ATOM	5552	CD2	LEU	A	726	9.813	26.053	25.542	1.00	47.46	A
ATOM	5553	C	LEU	A	726	8.584	22.397	27.844	1.00	53.00	A
ATOM	5554	O	LEU	A	726	8.942	22.414	29.019	1.00	53.00	A
ATOM	5555	N	ASN	A	727	8.288	21.271	27.189	1.00	53.74	A
ATOM	5556	CA	ASN	A	727	8.323	19.937	27.802	1.00	53.74	A
ATOM	5557	CB	ASN	A	727	7.077	19.153	27.384	1.00	71.67	A
ATOM	5558	CG	ASN	A	727	7.085	18.795	25.907	1.00	71.67	A
ATOM	5559	OD1	ASN	A	727	7.386	19.628	25.057	1.00	71.67	A
ATOM	5560	ND2	ASN	A	727	6.748	17.551	25.597	1.00	71.67	A
ATOM	5561	C	ASN	A	727	9.567	19.083	27.493	1.00	53.74	A
ATOM	5562	O	ASN	A	727	9.668	17.931	27.935	1.00	53.74	A
ATOM	5563	N	TYR	A	728	10.482	19.623	26.696	1.00	54.75	A
ATOM	5564	CA	TYR	A	728	11.730	18.928	26.378	1.00	54.75	A
ATOM	5565	CB	TYR	A	728	12.662	19.060	27.586	1.00	56.67	A
ATOM	5566	CG	TYR	A	728	12.969	20.502	27.924	1.00	56.67	A
ATOM	5567	CD1	TYR	A	728	14.024	21.172	27.302	1.00	56.67	A
ATOM	5568	CE1	TYR	A	728	14.284	22.502	27.570	1.00	56.67	A
ATOM	5569	CD2	TYR	A	728	12.178	21.211	28.827	1.00	56.67	A
ATOM	5570	CE2	TYR	A	728	12.427	22.550	29.100	1.00	56.67	A
ATOM	5571	CZ	TYR	A	728	13.484	23.186	28.469	1.00	56.67	A
ATOM	5572	OH	TYR	A	728	13.759	24.507	28.744	1.00	56.67	A
ATOM	5573	C	TYR	A	728	11.666	17.451	25.937	1.00	54.75	A
ATOM	5574	O	TYR	A	728	12.359	16.601	26.503	1.00	54.75	A
ATOM	5575	N	GLY	A	729	10.843	17.152	24.932	1.00	54.03	A
ATOM	5576	CA	GLY	A	729	10.749	15.788	24.426	1.00	54.03	A
ATOM	5577	C	GLY	A	729	9.915	14.783	25.208	1.00	54.03	A
ATOM	5578	O	GLY	A	729	9.689	13.665	24.738	1.00	54.03	A
ATOM	5579	N	SER	A	730	9.452	15.173	26.389	1.00	62.98	A
ATOM	5580	CA	SER	A	730	8.651	14.288	27.223	1.00	62.98	A
ATOM	5581	CB	SER	A	730	8.218	15.018	28.496	1.00	89.59	A
ATOM	5582	OG	SER	A	730	7.491	14.151	29.347	1.00	89.59	A
ATOM	5583	C	SER	A	730	7.415	13.766	26.481	1.00	62.98	A
ATOM	5584	O	SER	A	730	6.368	14.420	26.449	1.00	62.98	A
ATOM	5585	N	ILE	A	731	7.551	12.586	25.883	1.00	141.32	A
ATOM	5586	CA	ILE	A	731	6.449	11.974	25.153	1.00	141.32	A
ATOM	5587	CB	ILE	A	731	6.811	10.547	24.694	1.00	122.31	A
ATOM	5588	CG2	ILE	A	731	5.704	9.993	23.805	1.00	122.31	A
ATOM	5589	CG1	ILE	A	731	8.140	10.569	23.933	1.00	122.31	A
ATOM	5590	CD1	ILE	A	731	8.674	9.194	23.581	1.00	122.31	A
ATOM	5591	C	ILE	A	731	5.246	11.918	26.088	1.00	141.32	A
ATOM	5592	O	ILE	A	731	5.403	11.765	27.301	1.00	141.32	A
ATOM	5593	N	SER	A	732	4.049	12.047	25.523	1.00	191.41	A
ATOM	5594	CA	SER	A	732	2.821	12.035	26.310	1.00	191.41	A
ATOM	5595	CB	SER	A	732	2.764	10.790	27.203	1.00	119.32	A
ATOM	5596	OG	SER	A	732	2.817	9.604	26.430	1.00	119.32	A
ATOM	5597	C	SER	A	732	2.786	13.296	27.171	1.00	191.41	A
ATOM	5598	O	SER	A	732	2.926	13.233	28.393	1.00	191.41	A
ATOM	5599	N	ALA	A	733	2.606	14.440	26.517	1.00	174.30	A
ATOM	5600	CA	ALA	A	733	2.562	15.731	27.197	1.00	174.30	A
ATOM	5601	CB	ALA	A	733	2.309	16.843	26.182	1.00	95.05	A
ATOM	5602	C	ALA	A	733	1.505	15.777	28.297	1.00	174.30	A
ATOM	5603	O	ALA	A	733	0.314	15.939	28.026	1.00	174.30	A
ATOM	5604	N	ASP	A	734	1.953	15.636	29.540	1.00	130.52	A
ATOM	5605	CA	ASP	A	734	1.056	15.669	30.687	1.00	130.52	A
ATOM	5606	CB	ASP	A	734	1.081	14.325	31.415	1.00	142.65	A
ATOM	5607	CG	ASP	A	734	0.587	13.188	30.546	1.00	142.65	A

FIGURE 25 CON'T

```
ATOM   5608  OD1 ASP A 734      -0.587  13.230  30.123  1.00142.65      A
ATOM   5609  OD2 ASP A 734       1.374  12.254  30.284  1.00142.65      A
ATOM   5610  C   ASP A 734       1.469  16.783  31.640  1.00130.52      A
ATOM   5611  O   ASP A 734       0.830  17.001  32.671  1.00130.52      A
ATOM   5612  N   MSE A 735       2.544  17.484  31.286  1.00 83.68      A
ATOM   5613  CA  MSE A 735       3.045  18.586  32.100  1.00 83.68      A
ATOM   5614  CB  MSE A 735       4.291  19.200  31.441  1.00 77.09      A
ATOM   5615  CG  MSE A 735       5.145  20.077  32.359  1.00 77.09      A
ATOM   5616  SE  MSE A 735       6.711  20.840  31.466  1.00 77.09      A
ATOM   5617  CE  MSE A 735       7.603  19.190  30.986  1.00 77.09      A
ATOM   5618  C   MSE A 735       1.924  19.620  32.193  1.00 83.68      A
ATOM   5619  O   MSE A 735       1.658  20.350  31.239  1.00 83.68      A
ATOM   5620  N   ARG A 736       1.255  19.665  33.339  1.00 86.57      A
ATOM   5621  CA  ARG A 736       0.157  20.605  33.533  1.00 86.57      A
ATOM   5622  CB  ARG A 736      -0.890  20.006  34.483  1.00 66.03      A
ATOM   5623  CG  ARG A 736      -2.275  20.667  34.409  1.00 66.03      A
ATOM   5624  CD  ARG A 736      -3.147  20.224  35.570  1.00 66.03      A
ATOM   5625  NE  ARG A 736      -2.995  18.798  35.836  1.00 66.03      A
ATOM   5626  CZ  ARG A 736      -3.511  18.172  36.889  1.00 66.03      A
ATOM   5627  NH1 ARG A 736      -4.220  18.845  37.785  1.00 66.03      A
ATOM   5628  NH2 ARG A 736      -3.307  16.870  37.056  1.00 66.03      A
ATOM   5629  C   ARG A 736       0.655  21.927  34.109  1.00 86.57      A
ATOM   5630  O   ARG A 736      -0.139  22.821  34.395  1.00 86.57      A
ATOM   5631  N   LEU A 737       1.968  22.057  34.278  1.00 43.91      A
ATOM   5632  CA  LEU A 737       2.520  23.284  34.850  1.00 43.91      A
ATOM   5633  CB  LEU A 737       3.191  22.987  36.191  1.00 59.16      A
ATOM   5634  CG  LEU A 737       2.353  22.572  37.395  1.00 59.16      A
ATOM   5635  CD1 LEU A 737       3.286  22.259  38.543  1.00 59.16      A
ATOM   5636  CD2 LEU A 737       1.395  23.680  37.777  1.00 59.16      A
ATOM   5637  C   LEU A 737       3.531  23.980  33.977  1.00 43.91      A
ATOM   5638  O   LEU A 737       4.164  23.362  33.123  1.00 43.91      A
ATOM   5639  N   PRO A 738       3.680  25.299  34.163  1.00 43.31      A
ATOM   5640  CD  PRO A 738       2.886  26.184  35.032  1.00 37.96      A
ATOM   5641  CA  PRO A 738       4.653  26.073  33.386  1.00 43.31      A
ATOM   5642  CB  PRO A 738       4.562  27.454  34.021  1.00 37.96      A
ATOM   5643  CG  PRO A 738       3.115  27.525  34.416  1.00 37.96      A
ATOM   5644  C   PRO A 738       6.011  25.410  33.644  1.00 43.31      A
ATOM   5645  O   PRO A 738       6.336  25.082  34.786  1.00 43.31      A
ATOM   5646  N   ALA A 739       6.787  25.206  32.584  1.00 39.08      A
ATOM   5647  CA  ALA A 739       8.091  24.557  32.685  1.00 39.08      A
ATOM   5648  CB  ALA A 739       8.862  24.765  31.385  1.00 30.43      A
ATOM   5649  C   ALA A 739       8.949  25.001  33.878  1.00 39.08      A
ATOM   5650  O   ALA A 739       9.495  24.175  34.587  1.00 39.08      A
ATOM   5651  N   PRO A 740       9.082  26.315  34.111  1.00 39.59      A
ATOM   5652  CD  PRO A 740       8.523  27.468  33.389  1.00 52.42      A
ATOM   5653  CA  PRO A 740       9.908  26.752  35.246  1.00 39.59      A
ATOM   5654  CB  PRO A 740       9.718  28.268  35.246  1.00 52.42      A
ATOM   5655  CG  PRO A 740       9.456  28.572  33.791  1.00 52.42      A
ATOM   5656  C   PRO A 740       9.467  26.113  36.563  1.00 39.59      A
ATOM   5657  O   PRO A 740      10.289  25.636  37.345  1.00 39.59      A
ATOM   5658  N   VAL A 741       8.161  26.104  36.802  1.00 40.82      A
ATOM   5659  CA  VAL A 741       7.628  25.524  38.025  1.00 40.82      A

ATOM   5660  CB  VAL A 741       6.137  25.852  38.174  1.00 46.44      A
ATOM   5661  CG1 VAL A 741       5.582  25.217  39.450  1.00 46.44      A
ATOM   5662  CG2 VAL A 741       5.954  27.357  38.189  1.00 46.44      A
ATOM   5663  C   VAL A 741       7.799  24.010  38.012  1.00 40.82      A
```

FIGURE 25 CON'T

ATOM	5664	O	VAL	A	741	8.205	23.404	39.005	1.00	40.82	A
ATOM	5665	N	HIS	A	742	7.499	23.402	36.871	1.00	39.52	A
ATOM	5666	CA	HIS	A	742	7.608	21.961	36.747	1.00	39.52	A
ATOM	5667	CB	HIS	A	742	7.277	21.522	35.326	1.00	43.70	A
ATOM	5668	CG	HIS	A	742	7.385	20.046	35.122	1.00	43.70	A
ATOM	5669	CD2	HIS	A	742	6.528	19.043	35.422	1.00	43.70	A
ATOM	5670	ND1	HIS	A	742	8.490	19.451	34.551	1.00	43.70	A
ATOM	5671	CE1	HIS	A	742	8.306	18.143	34.504	1.00	43.70	A
ATOM	5672	NE2	HIS	A	742	7.123	17.870	35.029	1.00	43.70	A
ATOM	5673	C	HIS	A	742	8.994	21.464	37.105	1.00	39.52	A
ATOM	5674	O	HIS	A	742	9.147	20.554	37.914	1.00	39.52	A
ATOM	5675	N	TYR	A	743	10.010	22.063	36.494	1.00	38.31	A
ATOM	5676	CA	TYR	A	743	11.372	21.642	36.765	1.00	38.31	A
ATOM	5677	CB	TYR	A	743	12.289	22.174	35.658	1.00	45.12	A
ATOM	5678	CG	TYR	A	743	11.981	21.462	34.362	1.00	45.12	A
ATOM	5679	CD1	TYR	A	743	12.086	20.077	34.281	1.00	45.12	A
ATOM	5680	CE1	TYR	A	743	11.700	19.390	33.141	1.00	45.12	A
ATOM	5681	CD2	TYR	A	743	11.491	22.150	33.251	1.00	45.12	A
ATOM	5682	CE2	TYR	A	743	11.100	21.467	32.088	1.00	45.12	A
ATOM	5683	CZ	TYR	A	743	11.202	20.086	32.049	1.00	45.12	A
ATOM	5684	OH	TYR	A	743	10.755	19.382	30.953	1.00	45.12	A
ATOM	5685	C	TYR	A	743	11.856	21.998	38.169	1.00	38.31	A
ATOM	5686	O	TYR	A	743	12.664	21.277	38.747	1.00	38.31	A
ATOM	5687	N	ALA	A	744	11.359	23.088	38.736	1.00	40.59	A
ATOM	5688	CA	ALA	A	744	11.755	23.427	40.100	1.00	40.59	A
ATOM	5689	CB	ALA	A	744	11.083	24.719	40.549	1.00	43.93	A
ATOM	5690	C	ALA	A	744	11.318	22.265	41.001	1.00	40.59	A
ATOM	5691	O	ALA	A	744	12.074	21.802	41.861	1.00	40.59	A
ATOM	5692	N	HIS	A	745	10.101	21.782	40.775	1.00	40.98	A
ATOM	5693	CA	HIS	A	745	9.551	20.680	41.561	1.00	40.98	A
ATOM	5694	CB	HIS	A	745	8.069	20.465	41.212	1.00	68.13	A
ATOM	5695	CG	HIS	A	745	7.363	19.508	42.125	1.00	68.13	A
ATOM	5696	CD2	HIS	A	745	6.752	19.703	43.317	1.00	68.13	A
ATOM	5697	ND1	HIS	A	745	7.256	18.159	41.857	1.00	68.13	A
ATOM	5698	CE1	HIS	A	745	6.610	17.564	42.845	1.00	68.13	A
ATOM	5699	NE2	HIS	A	745	6.294	18.479	43.744	1.00	68.13	A
ATOM	5700	C	HIS	A	745	10.341	19.398	41.344	1.00	40.98	A
ATOM	5701	O	HIS	A	745	10.589	18.654	42.292	1.00	40.98	A
ATOM	5702	N	LYS	A	746	10.733	19.131	40.100	1.00	39.29	A
ATOM	5703	CA	LYS	A	746	11.513	17.932	39.819	1.00	39.29	A
ATOM	5704	CB	LYS	A	746	11.755	17.768	38.312	1.00	54.60	A
ATOM	5705	CG	LYS	A	746	10.509	17.447	37.497	1.00	54.60	A
ATOM	5706	CD	LYS	A	746	9.941	16.071	37.833	1.00	54.60	A
ATOM	5707	CE	LYS	A	746	10.830	14.954	37.303	1.00	54.60	A
ATOM	5708	NZ	LYS	A	746	10.225	13.592	37.502	1.00	54.60	A
ATOM	5709	C	LYS	A	746	12.862	18.008	40.538	1.00	39.29	A
ATOM	5710	O	LYS	A	746	13.337	17.019	41.070	1.00	39.29	A
ATOM	5711	N	PHE	A	747	13.488	19.179	40.543	1.00	36.74	A
ATOM	5712	CA	PHE	A	747	14.777	19.305	41.199	1.00	36.74	A
ATOM	5713	CB	PHE	A	747	15.427	20.646	40.860	1.00	40.07	A
ATOM	5714	CG	PHE	A	747	16.833	20.764	41.350	1.00	40.07	A
ATOM	5715	CD1	PHE	A	747	17.781	19.787	41.016	1.00	40.07	A
ATOM	5716	CD2	PHE	A	747	17.216	21.827	42.171	1.00	40.07	A
ATOM	5717	CE1	PHE	A	747	19.078	19.860	41.495	1.00	40.07	A
ATOM	5718	CE2	PHE	A	747	18.525	21.909	42.657	1.00	40.07	A
ATOM	5719	CZ	PHE	A	747	19.455	20.924	42.322	1.00	40.07	A
ATOM	5720	C	PHE	A	747	14.632	19.145	42.724	1.00	36.74	A

FIGURE 25 CON'T

```
ATOM   5721  O   PHE A 747      15.399  18.411  43.354  1.00 36.74      A
ATOM   5722  N   ALA A 748      13.643  19.811  43.306  1.00 44.70      A
ATOM   5723  CA  ALA A 748      13.406  19.694  44.737  1.00 44.70      A
ATOM   5724  CB  ALA A 748      12.158  20.491  45.134  1.00 34.75      A
ATOM   5725  C   ALA A 748      13.222  18.204  45.062  1.00 44.70      A
ATOM   5726  O   ALA A 748      13.719  17.719  46.072  1.00 44.70      A
ATOM   5727  N   ASN A 749      12.529  17.476  44.192  1.00 45.21      A
ATOM   5728  CA  ASN A 749      12.324  16.045  44.410  1.00 45.21      A
ATOM   5729  CB  ASN A 749      11.366  15.457  43.368  1.00 59.26      A
ATOM   5730  CG  ASN A 749       9.913  15.757  43.675  1.00 59.26      A
ATOM   5731  OD1 ASN A 749       9.553  16.036  44.821  1.00 59.26      A
ATOM   5732  ND2 ASN A 749       9.064  15.681  42.655  1.00 59.26      A
ATOM   5733  C   ASN A 749      13.627  15.245  44.380  1.00 45.21      A
ATOM   5734  O   ASN A 749      13.850  14.374  45.223  1.00 45.21      A
ATOM   5735  N   ALA A 750      14.479  15.529  43.402  1.00 49.51      A
ATOM   5736  CA  ALA A 750      15.746  14.822  43.274  1.00 49.51      A
ATOM   5737  CB  ALA A 750      16.437  15.231  41.979  1.00 33.70      A
ATOM   5738  C   ALA A 750      16.658  15.085  44.482  1.00 49.51      A
ATOM   5739  O   ALA A 750      17.362  14.185  44.950  1.00 49.51      A
ATOM   5740  N   ILE A 751      16.648  16.315  44.980  1.00 50.38      A
ATOM   5741  CA  ILE A 751      17.459  16.662  46.144  1.00 50.38      A
ATOM   5742  CB  ILE A 751      17.342  18.166  46.510  1.00 52.88      A
ATOM   5743  CG2 ILE A 751      18.258  18.485  47.690  1.00 52.88      A
ATOM   5744  CG1 ILE A 751      17.759  19.040  45.336  1.00 52.88      A
ATOM   5745  CD1 ILE A 751      17.551  20.509  45.594  1.00 52.88      A
ATOM   5746  C   ILE A 751      16.957  15.843  47.341  1.00 50.38      A
ATOM   5747  O   ILE A 751      17.752  15.317  48.123  1.00 50.38      A
ATOM   5748  N   ARG A 752      15.635  15.745  47.475  1.00 59.72      A
ATOM   5749  CA  ARG A 752      15.033  14.983  48.564  1.00 59.72      A
ATOM   5750  CB  ARG A 752      13.522  15.228  48.652  1.00 91.88      A
ATOM   5751  CG  ARG A 752      13.114  16.607  49.133  1.00 91.88      A
ATOM   5752  CD  ARG A 752      11.888  16.535  50.036  1.00 91.88      A
ATOM   5753  NE  ARG A 752      10.793  15.787  49.427  1.00 91.88      A
ATOM   5754  CZ  ARG A 752      10.169  16.149  48.310  1.00 91.88      A
ATOM   5755  NH1 ARG A 752      10.528  17.257  47.675  1.00 91.88      A
ATOM   5756  NH2 ARG A 752       9.186  15.400  47.825  1.00 91.88      A
ATOM   5757  C   ARG A 752      15.268  13.494  48.365  1.00 59.72      A
ATOM   5758  O   ARG A 752      15.139  12.718  49.306  1.00 59.72      A
ATOM   5759  N   ASN A 753      15.603  13.096  47.138  1.00 55.46      A
ATOM   5760  CA  ASN A 753      15.845  11.688  46.848  1.00 55.46      A
ATOM   5761  CB  ASN A 753      15.153  11.276  45.545  1.00 64.92      A
ATOM   5762  CG  ASN A 753      13.645  11.126  45.707  1.00 64.92      A
ATOM   5763  OD1 ASN A 753      13.170  10.514  46.668  1.00 64.92      A
ATOM   5764  ND2 ASN A 753      12.888  11.670  44.758  1.00 64.92      A
ATOM   5765  C   ASN A 753      17.322  11.304  46.804  1.00 55.46      A
ATOM   5766  O   ASN A 753      17.673  10.220  46.344  1.00 55.46      A
ATOM   5767  N   GLU A 754      18.185  12.199  47.273  1.00 51.88      A
ATOM   5768  CA  GLU A 754      19.623  11.921  47.347  1.00 51.88      A
ATOM   5769  CB  GLU A 754      19.856  10.502  47.891  1.00 96.52      A
ATOM   5770  CG  GLU A 754      19.132  10.172  49.191  1.00 96.52      A
ATOM   5771  CD  GLU A 754      19.887  10.626  50.423  1.00 96.52      A
ATOM   5772  OE1 GLU A 754      21.018  10.141  50.641  1.00 96.52      A
ATOM   5773  OE2 GLU A 754      19.348  11.464  51.176  1.00 96.52      A
ATOM   5774  C   GLU A 754      20.425  12.077  46.054  1.00 51.88      A
ATOM   5775  O   GLU A 754      21.491  11.475  45.912  1.00 51.88      A
ATOM   5776  N   TRP A 755      19.928  12.859  45.104  1.00 47.41      A
ATOM   5777  CA  TRP A 755      20.682  13.044  43.871  1.00 47.41      A
```

FIGURE 25 CON'T

```
ATOM   5778  CB  TRP A 755      19.811  13.659  42.772  1.00 40.13      A
ATOM   5779  CG  TRP A 755      19.004  12.671  41.988  1.00 40.13      A
ATOM   5780  CD2 TRP A 755      19.229  12.278  40.630  1.00 40.13      A
ATOM   5781  CE2 TRP A 755      18.178  11.398  40.267  1.00 40.13      A
ATOM   5782  CE3 TRP A 755      20.214  12.588  39.681  1.00 40.13      A
ATOM   5783  CD1 TRP A 755      17.860  12.024  42.392  1.00 40.13      A
ATOM   5784  NE1 TRP A 755      17.357  11.260  41.359  1.00 40.13      A
ATOM   5785  CZ2 TRP A 755      18.084  10.831  38.991  1.00 40.13      A
ATOM   5786  CZ3 TRP A 755      20.122  12.024  38.407  1.00 40.13      A
ATOM   5787  CH2 TRP A 755      19.061  11.154  38.076  1.00 40.13      A

ATOM   5788  C   TRP A 755      21.858  13.968  44.130  1.00 47.41      A
ATOM   5789  O   TRP A 755      21.746  14.930  44.891  1.00 47.41      A
ATOM   5790  N   LYS A 756      22.989  13.680  43.502  1.00 47.96      A
ATOM   5791  CA  LYS A 756      24.144  14.543  43.666  1.00 47.96      A
ATOM   5792  CB  LYS A 756      25.363  13.980  42.935  1.00 56.84      A
ATOM   5793  CG  LYS A 756      26.597  14.853  43.110  1.00 56.84      A
ATOM   5794  CD  LYS A 756      27.900  14.128  42.787  1.00 56.84      A
ATOM   5795  CE  LYS A 756      28.049  13.833  41.307  1.00 56.84      A
ATOM   5796  NZ  LYS A 756      29.380  13.233  41.026  1.00 56.84      A
ATOM   5797  C   LYS A 756      23.784  15.914  43.085  1.00 47.96      A
ATOM   5798  O   LYS A 756      23.029  16.015  42.116  1.00 47.96      A
ATOM   5799  N   ILE A 757      24.326  16.966  43.677  1.00 58.56      A
ATOM   5800  CA  ILE A 757      24.059  18.316  43.214  1.00 58.56      A
ATOM   5801  CB  ILE A 757      23.677  19.206  44.410  1.00 46.28      A
ATOM   5802  CG2 ILE A 757      23.447  20.644  43.964  1.00 46.28      A
ATOM   5803  CG1 ILE A 757      22.424  18.621  45.072  1.00 46.28      A
ATOM   5804  CD1 ILE A 757      21.869  19.432  46.241  1.00 46.28      A
ATOM   5805  C   ILE A 757      25.278  18.878  42.479  1.00 58.56      A
ATOM   5806  O   ILE A 757      26.110  19.555  43.078  1.00 58.56      A
ATOM   5807  N   LYS A 758      25.381  18.585  41.182  1.00 49.81      A
ATOM   5808  CA  LYS A 758      26.502  19.063  40.368  1.00 49.81      A
ATOM   5809  CB  LYS A 758      26.704  18.174  39.137  1.00 73.65      A
ATOM   5810  CG  LYS A 758      27.420  16.873  39.416  1.00 73.65      A
ATOM   5811  CD  LYS A 758      28.857  17.110  39.850  1.00 73.65      A
ATOM   5812  CE  LYS A 758      29.724  17.530  38.678  1.00 73.65      A
ATOM   5813  NZ  LYS A 758      29.896  16.415  37.724  1.00 73.65      A
ATOM   5814  C   LYS A 758      26.264  20.487  39.905  1.00 49.81      A
ATOM   5815  O   LYS A 758      25.772  20.709  38.797  1.00 49.81      A
ATOM   5816  N   GLU A 759      26.634  21.452  40.736  1.00 45.60      A
ATOM   5817  CA  GLU A 759      26.420  22.853  40.387  1.00 45.60      A
ATOM   5818  CB  GLU A 759      26.965  23.754  41.492  1.00 52.93      A
ATOM   5819  CG  GLU A 759      26.155  23.586  42.767  1.00 52.93      A
ATOM   5820  CD  GLU A 759      26.388  24.667  43.792  1.00 52.93      A
ATOM   5821  OE1 GLU A 759      25.624  24.695  44.782  1.00 52.93      A
ATOM   5822  OE2 GLU A 759      27.324  25.481  43.619  1.00 52.93      A
ATOM   5823  C   GLU A 759      26.993  23.215  39.027  1.00 45.60      A
ATOM   5824  O   GLU A 759      26.477  24.097  38.338  1.00 45.60      A
ATOM   5825  N   GLU A 760      28.037  22.508  38.625  1.00 50.56      A
ATOM   5826  CA  GLU A 760      28.656  22.745  37.329  1.00 50.56      A
ATOM   5827  CB  GLU A 760      29.829  21.788  37.154  1.00 77.81      A
ATOM   5828  CG  GLU A 760      30.544  21.897  35.829  1.00 77.81      A
ATOM   5829  CD  GLU A 760      31.612  20.831  35.681  1.00 77.81      A
ATOM   5830  OE1 GLU A 760      32.504  20.760  36.554  1.00 77.81      A
ATOM   5831  OE2 GLU A 760      31.560  20.062  34.699  1.00 77.81      A
ATOM   5832  C   GLU A 760      27.626  22.516  36.211  1.00 50.56      A
ATOM   5833  O   GLU A 760      27.507  23.306  35.274  1.00 50.56      A
```

FIGURE 25 CON'T

ATOM	5834	N	PHE	A	761	26.888	21.415	36.312	1.00	40.45	A
ATOM	5835	CA	PHE	A	761	25.872	21.089	35.314	1.00	40.45	A
ATOM	5836	CB	PHE	A	761	25.491	19.603	35.421	1.00	46.40	A
ATOM	5837	CG	PHE	A	761	26.577	18.667	34.961	1.00	46.40	A
ATOM	5838	CD1	PHE	A	761	27.811	19.165	34.527	1.00	46.40	A
ATOM	5839	CD2	PHE	A	761	26.368	17.293	34.944	1.00	46.40	A
ATOM	5840	CE1	PHE	A	761	28.813	18.308	34.082	1.00	46.40	A
ATOM	5841	CE2	PHE	A	761	27.366	16.418	34.500	1.00	46.40	A
ATOM	5842	CZ	PHE	A	761	28.596	16.931	34.066	1.00	46.40	A
ATOM	5843	C	PHE	A	761	24.641	21.972	35.490	1.00	40.45	A
ATOM	5844	O	PHE	A	761	24.097	22.485	34.521	1.00	40.45	A
ATOM	5845	N	LEU	A	762	24.233	22.168	36.737	1.00	42.78	A
ATOM	5846	CA	LEU	A	762	23.064	22.977	37.058	1.00	42.78	A
ATOM	5847	CB	LEU	A	762	22.803	22.911	38.568	1.00	39.89	A
ATOM	5848	CG	LEU	A	762	22.567	21.510	39.164	1.00	39.89	A
ATOM	5849	CD1	LEU	A	762	22.491	21.589	40.699	1.00	39.89	A
ATOM	5850	CD2	LEU	A	762	21.276	20.912	38.584	1.00	39.89	A
ATOM	5851	C	LEU	A	762	23.186	24.444	36.613	1.00	42.78	A
ATOM	5852	O	LEU	A	762	22.168	25.115	36.361	1.00	42.78	A
ATOM	5853	N	ALA	A	763	24.423	24.936	36.514	1.00	43.71	A
ATOM	5854	CA	ALA	A	763	24.679	26.319	36.116	1.00	43.71	A
ATOM	5855	CB	ALA	A	763	26.098	26.736	36.552	1.00	50.06	A
ATOM	5856	C	ALA	A	763	24.510	26.537	34.614	1.00	43.71	A
ATOM	5857	O	ALA	A	763	24.491	27.674	34.139	1.00	43.71	A
ATOM	5858	N	GLU	A	764	24.398	25.442	33.870	1.00	43.52	A
ATOM	5859	CA	GLU	A	764	24.222	25.509	32.425	1.00	43.52	A
ATOM	5860	CB	GLU	A	764	25.292	24.665	31.727	1.00	62.60	A
ATOM	5861	CG	GLU	A	764	26.693	25.246	31.815	1.00	62.60	A
ATOM	5862	CD	GLU	A	764	26.866	26.463	30.932	1.00	62.60	A
ATOM	5863	OE1	GLU	A	764	27.217	26.298	29.743	1.00	62.60	A
ATOM	5864	OE2	GLU	A	764	26.632	27.587	31.425	1.00	62.60	A
ATOM	5865	C	GLU	A	764	22.831	24.989	32.064	1.00	43.52	A
ATOM	5866	O	GLU	A	764	22.534	24.737	30.903	1.00	43.52	A
ATOM	5867	N	GLY	A	765	21.988	24.806	33.074	1.00	40.66	A
ATOM	5868	CA	GLY	A	765	20.648	24.324	32.810	1.00	40.66	A
ATOM	5869	C	GLY	A	765	20.502	22.858	32.430	1.00	40.66	A
ATOM	5870	O	GLY	A	765	19.542	22.506	31.748	1.00	40.66	A
ATOM	5871	N	PHE	A	766	21.442	22.013	32.859	1.00	37.82	A
ATOM	5872	CA	PHE	A	766	21.389	20.572	32.582	1.00	37.82	A
ATOM	5873	CB	PHE	A	766	22.663	19.857	33.076	1.00	44.51	A
ATOM	5874	CG	PHE	A	766	23.860	19.974	32.170	1.00	44.51	A
ATOM	5875	CD1	PHE	A	766	24.322	21.210	31.730	1.00	44.51	A
ATOM	5876	CD2	PHE	A	766	24.597	18.834	31.846	1.00	44.51	A
ATOM	5877	CE1	PHE	A	766	25.509	21.310	30.983	1.00	44.51	A
ATOM	5878	CE2	PHE	A	766	25.778	18.922	31.104	1.00	44.51	A
ATOM	5879	CZ	PHE	A	766	26.236	20.162	30.674	1.00	44.51	A
ATOM	5880	C	PHE	A	766	20.218	19.952	33.367	1.00	37.82	A
ATOM	5881	O	PHE	A	766	20.238	19.949	34.598	1.00	37.82	A
ATOM	5882	N	LEU	A	767	19.209	19.418	32.686	1.00	38.39	A
ATOM	5883	CA	LEU	A	767	18.103	18.782	33.412	1.00	38.39	A
ATOM	5884	CB	LEU	A	767	16.802	18.925	32.616	1.00	34.83	A
ATOM	5885	CG	LEU	A	767	16.252	20.355	32.537	1.00	34.83	A
ATOM	5886	CD1	LEU	A	767	15.172	20.439	31.471	1.00	34.83	A
ATOM	5887	CD2	LEU	A	767	15.711	20.772	33.909	1.00	34.83	A
ATOM	5888	C	LEU	A	767	18.454	17.302	33.609	1.00	38.39	A
ATOM	5889	O	LEU	A	767	17.730	16.404	33.154	1.00	38.39	A
ATOM	5890	N	TYR	A	768	19.560	17.041	34.307	1.00	32.98	A

FIGURE 25 CON'T

```
ATOM   5891  CA  TYR A 768      20.016  15.655  34.494  1.00 32.98      A
ATOM   5892  CB  TYR A 768      21.479  15.628  34.948  1.00 37.63      A
ATOM   5893  CG  TYR A 768      21.718  16.219  36.318  1.00 37.63      A
ATOM   5894  CD1 TYR A 768      21.427  15.499  37.479  1.00 37.63      A
ATOM   5895  CE1 TYR A 768      21.680  16.036  38.742  1.00 37.63      A
ATOM   5896  CD2 TYR A 768      22.266  17.492  36.454  1.00 37.63      A
ATOM   5897  CE2 TYR A 768      22.527  18.034  37.705  1.00 37.63      A
ATOM   5898  CZ  TYR A 768      22.233  17.310  38.845  1.00 37.63      A
ATOM   5899  OH  TYR A 768      22.488  17.874  40.081  1.00 37.63      A
ATOM   5900  C   TYR A 768      19.206  14.799  35.440  1.00 32.98      A
ATOM   5901  O   TYR A 768      19.243  13.579  35.338  1.00 32.98      A
ATOM   5902  N   PHE A 769      18.486  15.443  36.352  1.00 42.84      A
ATOM   5903  CA  PHE A 769      17.663  14.769  37.349  1.00 42.84      A
ATOM   5904  CB  PHE A 769      17.633  15.633  38.604  1.00 31.31      A
ATOM   5905  CG  PHE A 769      17.232  17.052  38.325  1.00 31.31      A
ATOM   5906  CD1 PHE A 769      15.885  17.417  38.284  1.00 31.31      A
ATOM   5907  CD2 PHE A 769      18.194  17.997  37.962  1.00 31.31      A
ATOM   5908  CE1 PHE A 769      15.505  18.686  37.881  1.00 31.31      A
ATOM   5909  CE2 PHE A 769      17.819  19.269  37.556  1.00 31.31      A
ATOM   5910  CZ  PHE A 769      16.471  19.616  37.513  1.00 31.31      A
ATOM   5911  C   PHE A 769      16.224  14.553  36.851  1.00 42.84      A
ATOM   5912  O   PHE A 769      15.406  13.941  37.540  1.00 42.84      A
ATOM   5913  N   VAL A 770      15.923  15.068  35.664  1.00 74.51      A
ATOM   5914  CA  VAL A 770      14.588  14.955  35.092  1.00 74.51      A
ATOM   5915  CB  VAL A 770      14.200  16.229  34.315  1.00 61.33      A

ATOM   5916  CG1 VAL A 770      12.799  16.097  33.781  1.00 61.33      A
ATOM   5917  CG2 VAL A 770      14.301  17.436  35.202  1.00 61.33      A
ATOM   5918  C   VAL A 770      14.477  13.785  34.132  1.00 74.51      A
ATOM   5919  O   VAL A 770      14.621  14.045  32.917  1.00 74.51      A
ATOM   5920  OXT VAL A 770      14.260  12.640  34.588  1.00 61.33      A
TER
HETATM 5921  OH2 TIP     1      18.370  21.810  29.334  1.00 44.97      S
HETATM 5922  OH2 TIP     2      21.899   9.099  35.356  1.00 40.25      S
HETATM 5923  OH2 TIP     3      17.715  23.135  26.861  1.00 45.74      S
HETATM 5924  OH2 TIP     4      -2.476  34.389  46.433  1.00 57.89      S
HETATM 5925  OH2 TIP     5     -14.987   6.046  36.915  1.00 53.30      S
HETATM 5926  OH2 TIP     6     -12.088  26.903  41.491  1.00 46.69      S
HETATM 5927  OH2 TIP     7     -13.937  25.878  43.376  1.00 45.40      S
HETATM 5928  OH2 TIP     8     -11.412  13.515  38.333  1.00 43.19      S
HETATM 5929  OH2 TIP     9      -0.863  24.163  41.344  1.00 53.53      S
HETATM 5930  OH2 TIP    10      -5.288   1.461  64.019  1.00 48.92      S
HETATM 5931  OH2 TIP    11       2.392  30.592  41.077  1.00 38.99      S
HETATM 5932  OH2 TIP    12      -0.342   0.215  47.316  1.00 46.86      S
HETATM 5933  OH2 TIP    13      -9.647  15.151  37.001  1.00 45.57      S
HETATM 5934  OH2 TIP    14     -10.301  15.778  34.084  1.00 43.77      S
HETATM 5935  OH2 TIP    15      20.555  11.259  34.330  1.00 45.20      S
HETATM 5936  OH2 TIP    16      28.742  20.816  42.795  1.00 44.99      S
HETATM 5937  OH2 TIP    17     -13.195  30.515  39.458  1.00 52.48      S
HETATM 5938  OH2 TIP    18     -11.704  20.891  31.112  1.00 42.42      S
HETATM 5939  OH2 TIP    19      -3.276   9.798  47.460  1.00 49.11      S
HETATM 5940  OH2 TIP    20      -6.804   0.216  75.536  1.00 47.88      S
HETATM 5941  OH2 TIP    21     -18.325  20.403  49.558  1.00 50.84      S
HETATM 5942  OH2 TIP    22     -16.649  26.665  47.872  1.00 47.40      S
HETATM 5943  OH2 TIP    23     -16.485  13.068  25.192  1.00 47.13      S
HETATM 5944  OH2 TIP    24     -18.046   8.967  49.052  1.00 49.94      S
HETATM 5945  OH2 TIP    25       9.520  -9.191  28.429  1.00 58.22      S
```

FIGURE 25 CON'T

```
HETATM 5946  OH2 TIP    26      16.540  25.632  27.261  1.00 47.57      S
HETATM 5947  OH2 TIP    27       3.118  37.550  32.058  1.00 54.40      S
HETATM 5948  OH2 TIP    28      10.045  -3.931  55.270  1.00 51.11      S
HETATM 5949  OH2 TIP    29      15.202   8.781  31.435  1.00 49.91      S
HETATM 5950  OH2 TIP    30     -26.959  25.672  35.586  1.00 48.67      S
HETATM 5951  OH2 TIP    31      10.791  -9.014  26.464  1.00 59.29      S
HETATM 5952  OH2 TIP    32      -2.669  23.392  42.935  1.00 57.01      S
HETATM 5953  OH2 TIP    33     -19.309  21.014  25.827  1.00 48.36      S
HETATM 5954  OH2 TIP    34      -9.112  11.965  44.438  1.00 56.44      S
HETATM 5955  OH2 TIP    35     -26.009  29.088  33.535  1.00 53.75      S
HETATM 5956  OH2 TIP    36      -5.553   4.212  66.054  1.00 69.21      S
HETATM 5957  OH2 TIP    37      11.338  20.488  23.113  1.00 57.25      S
HETATM 5958  OH2 TIP    38      -9.515  16.282  40.382  1.00 53.65      S
HETATM 5959  OH2 TIP    39       2.189   8.728  53.259  1.00 51.62      S
HETATM 5960  OH2 TIP    40      29.893  20.655  40.220  1.00 61.64      S
HETATM 5961  OH2 TIP    41      -8.168  36.508  40.351  1.00 56.55      S
HETATM 5962  OH2 TIP    42     -16.396  37.700  39.050  1.00 57.28      S
HETATM 5963  OH2 TIP    43     -17.803  38.142  41.395  1.00 62.91      S
HETATM 5964  OH2 TIP    44       6.251   7.179  47.328  1.00 50.89      S
HETATM 5965  OH2 TIP    45      -7.728  22.337  20.181  1.00 51.49      S
HETATM 5966  OH2 TIP    46       6.036  24.040  46.517  1.00 57.58      S
HETATM 5967  OH2 TIP    47     -10.838  11.111  57.417  1.00 72.00      S
HETATM 5968  OH2 TIP    48       9.902   4.698  27.131  1.00 54.85      S
HETATM 5969  OH2 TIP    49      24.470  32.001  48.942  1.00 64.93      S
HETATM 5970  OH2 TIP    50      21.439  27.832  48.102  1.00 55.84      S
HETATM 5971  OH2 TIP    51     -23.212   4.269  47.464  1.00 52.89      S
HETATM 5972  OH2 TIP    52       8.541   4.628  44.863  1.00 68.12      S
HETATM 5973  OH2 TIP    53     -16.370  13.072  47.759  1.00 51.09      S
HETATM 5974  OH2 TIP    54       9.141  18.845  46.330  1.00 55.16      S
HETATM 5975  OH2 TIP    55     -21.814   2.461  46.114  1.00 61.78      S
HETATM 5976  OH2 TIP    56     -28.157  10.364  48.240  1.00 53.11      S
HETATM 5977  OH2 TIP    57     -27.342  32.420  42.439  1.00 51.52      S
HETATM 5978  OH2 TIP    58     -15.983  27.483  57.654  1.00 55.12      S
HETATM 5979  OH2 TIP    59     -16.252  16.477  36.469  1.00 22.88      S
HETATM 5980  OH2 TIP    60      16.220  10.260   4.698  1.00 70.64      S
HETATM 5981  OH2 TIP    61       9.900   7.126  48.174  1.00 69.93      S
HETATM 5982  OH2 TIP    62      -2.545  14.634  63.859  1.00 66.97      S
HETATM 5983  OH2 TIP    63     -25.196   4.635  45.535  1.00 51.71      S
HETATM 5984  OH2 TIP    64     -18.872  -1.352  47.305  1.00 70.97      S
HETATM 5985  OH2 TIP    65       2.709 -12.794  61.990  1.00 71.93      S
HETATM 5986  OH2 TIP    66     -11.260  -6.365  37.836  1.00 73.76      S
HETATM 5987  OH2 TIP    67     -15.786  37.673  36.314  1.00 74.43      S
HETATM 5988  OH2 TIP    68      17.880  22.397  16.014  1.00 54.49      S
HETATM 5989  OH2 TIP    69     -21.502  15.816  52.789  1.00 56.42      S
HETATM 5990  OH2 TIP    70       5.325  -0.467  16.696  1.00 60.24      S
HETATM 5991  OH2 TIP    71      11.117  22.339  24.819  1.00 61.70      S
HETATM 5992  OH2 TIP    72      23.110  11.363  42.088  1.00 46.89      S
HETATM 5993  OH2 TIP    73      21.863  -9.662  36.508  1.00 47.82      S
HETATM 5994  OH2 TIP    74      20.547  46.701  40.738  1.00 72.58      S
HETATM 5995  OH2 TIP    75      33.405   9.009  38.372  1.00 64.06      S
HETATM 5996  OH2 TIP    76      -7.459  19.056  39.490  1.00 53.56      S
HETATM 5997  OH2 TIP    77     -16.279  32.467  44.564  1.00 54.71      S
HETATM 5998  OH2 TIP    78      20.859  37.282  41.728  1.00 53.34      S
HETATM 5999  OH2 TIP    79      -9.099   5.768  64.065  1.00 53.69      S
HETATM 6000  OH2 TIP    80      17.074  48.531  37.844  1.00 57.71      S
HETATM 6001  OH2 TIP    81     -20.591   1.700  36.204  1.00 54.39      S
HETATM 6002  OH2 TIP    82      28.187  29.184  34.781  1.00 68.56      S
```

FIGURE 25 CON'T

```
HETATM 6003  OH2 TIP    83      17.032  36.198  26.598  1.00 67.39      S
HETATM 6004  OH2 TIP    84      22.262   8.106  13.250  1.00 55.06      S
HETATM 6005  OH2 TIP    85      21.630  15.662  15.725  1.00 70.89      S
HETATM 6006  OH2 TIP    86     -14.521   1.762  54.240  1.00 56.21      S
HETATM 6007  OH2 TIP    87      -5.498  -7.282  59.486  1.00 64.11      S
HETATM 6008  OH2 TIP    88     -14.952  27.909  45.106  1.00 55.41      S
HETATM 6009  OH2 TIP    89      -9.574  11.072  36.645  1.00 60.66      S
HETATM 6010  OH2 TIP    90     -19.934  26.786  19.690  1.00 61.56      S
HETATM 6011  OH2 TIP    91     -19.722  25.179  57.795  1.00 61.53      S
HETATM 6012  OH2 TIP    92      -5.179   4.991  79.116  1.00 59.85      S
HETATM 6013  OH2 TIP    93      23.200  29.231  31.436  1.00 56.39      S
HETATM 6014  OH2 TIP    94      14.477  10.996  37.967  1.00 62.57      S
HETATM 6015  OH2 TIP    95       5.075  38.959  28.482  1.00 60.07      S
HETATM 6016  OH2 TIP    96       3.783  42.153  55.054  1.00 83.33      S
HETATM 6017  OH2 TIP    97       4.878  29.768  52.759  1.00 52.19      S
HETATM 6018  OH2 TIP    98     -28.304  35.106  42.428  1.00 68.52      S
HETATM 6019  OH2 TIP    99      -6.647 -10.395  70.918  1.00 54.01      S
HETATM 6020  OH2 TIP   100     -21.038  41.643  47.045  1.00 67.28      S
HETATM 6021  OH2 TIP   101      34.025   6.004  38.783  1.00 54.10      S
HETATM 6022  OH2 TIP   102      36.250   4.424  29.906  1.00 61.46      S
HETATM 6023  OH2 TIP   103     -19.532  -2.215  42.785  1.00 68.84      S
HETATM 6024  OH2 TIP   104     -28.578  38.820  54.834  1.00 61.91      S
HETATM 6025  OH2 TIP   105     -31.547  35.211  67.941  1.00 72.99      S
HETATM 6026  OH2 TIP   106      25.271  22.710  46.374  1.00 68.08      S
HETATM 6027  OH2 TIP   107     -25.496  28.500  31.122  1.00 51.94      S
HETATM 6028  OH2 TIP   108      30.641  -4.118  25.389  1.00 61.56      S
HETATM 6029  OH2 TIP   109     -10.470  12.483  33.234  1.00 29.98      S
HETATM 6030  OH2 TIP   110      -1.801  12.520  50.029  1.00 74.36      S
HETATM 6031  OH2 TIP   111       6.173  25.074  43.601  1.00 49.94      S
HETATM 6032  OH2 TIP   112      20.958 -10.184  22.202  1.00 80.32      S
HETATM 6033  OH2 TIP   113      22.035  25.421  55.991  1.00 64.77      S
HETATM 6034  OH2 TIP   114     -30.415  16.042  33.842  1.00 57.83      S
HETATM 6035  OH2 TIP   115       5.151  24.111  49.267  1.00 58.42      S
HETATM 6036  OH2 TIP   116     -12.603   7.930  52.673  1.00 59.27      S
HETATM 6037  OH2 TIP   117      27.059 -10.195  35.988  1.00 57.86      S
HETATM 6038  OH2 TIP   118      -3.826  -5.899  43.779  1.00 51.76      S
HETATM 6039  OH2 TIP   119      -4.725  20.658  29.307  1.00 62.77      S
HETATM 6040  OH2 TIP   120     -18.107  11.820  49.900  1.00 68.29      S
HETATM 6041  OH2 TIP   121      17.151  11.758  34.731  1.00 55.47      S
HETATM 6042  OH2 TIP   122       8.014  33.927  55.929  1.00 71.42      S
HETATM 6043  OH2 TIP   123      -3.700  -4.366  41.096  1.00 77.33      S
HETATM 6044  OH2 TIP   124       0.364  19.226  44.509  1.00 61.07      S
HETATM 6045  OH2 TIP   125     -24.577  17.454  58.370  1.00 86.24      S
HETATM 6046  OH2 TIP   126      22.736  -8.506  25.854  1.00 56.67      S
HETATM 6047  OH2 TIP   127       7.925  -9.335  64.313  1.00 77.83      S
HETATM 6048  OH2 TIP   128       0.340  27.055  48.265  1.00 63.16      S
HETATM 6049  OH2 TIP   129      -3.152  41.692  27.224  1.00 52.94      S
HETATM 6050  OH2 TIP   130     -31.945  32.910  40.837  1.00 57.78      S
HETATM 6051  OH2 TIP   131      16.495  37.467  29.440  1.00 60.34      S
HETATM 6052  OH2 TIP   132      -9.277  38.782  34.372  1.00 67.29      S
HETATM 6053  OH2 TIP   133      -1.692  32.663  53.014  1.00 71.19      S
HETATM 6054  OH2 TIP   134     -15.239  34.373  42.234  1.00 64.11      S
HETATM 6055  OH2 TIP   135       9.945  15.897  33.414  1.00 70.18      S
HETATM 6056  OH2 TIP   136      26.089  32.855  33.020  1.00 73.49      S
HETATM 6057  OH2 TIP   137      -1.929  26.327  46.767  1.00 64.01      S
HETATM 6058  OH2 TIP   138      13.583  11.648  31.478  1.00 60.15      S
HETATM 6059  OH2 TIP   139      -7.307  -6.874  73.320  1.00 63.01      S
```

FIGURE 25 CON'T

```
HETATM 6060  OH2 TIP   140       9.685  -0.304  44.722  1.00 73.65      S
HETATM 6061  OH2 TIP   141      -9.735  19.821  43.417  1.00 71.29      S
HETATM 6062  OH2 TIP   142      13.163  34.923  21.459  1.00 68.38      S
HETATM 6063  OH2 TIP   143      26.022  30.090  31.402  1.00 68.11      S
HETATM 6064  OH2 TIP   144     -27.679   1.275  40.061  1.00 63.18      S
HETATM 6065  OH2 TIP   145      14.352  31.000  21.838  1.00 55.20      S
HETATM 6066  OH2 TIP   146       2.168  46.394  49.629  1.00 60.35      S
HETATM 6067  OH2 TIP   147      17.351   9.774  33.057  1.00 69.92      S
HETATM 6068  OH2 TIP   148      22.741  27.792  29.446  1.00 67.41      S
HETATM 6069  OH2 TIP   149      25.467  17.052  46.437  1.00 51.85      S
HETATM 6070  OH2 TIP   150      -8.133  12.899  35.603  1.00 51.72      S
HETATM 6071  OH2 TIP   151      39.496  12.986  32.142  1.00 62.69      S
HETATM 6072  OH2 TIP   152     -27.004  20.006  31.382  1.00 55.79      S
HETATM 6073  OH2 TIP   153      11.578  47.500  43.124  1.00 55.79      S
HETATM 6074  OH2 TIP   154     -20.336  32.675  28.580  1.00 55.17      S
HETATM 6075  OH2 TIP   155      13.097 -10.641  36.782  1.00 68.86      S
HETATM 6076  OH2 TIP   156       5.383   2.741  40.628  1.00 76.91      S
HETATM 6077  OH2 TIP   157       0.299  -0.391  44.871  1.00 75.15      S
HETATM 6078  OH2 TIP   158      18.732  30.891  19.910  1.00 57.45      S
HETATM 6079  OH2 TIP   159      11.519  16.830  31.002  1.00 66.16      S
HETATM 6080  OH2 TIP   160       5.770  13.582  62.799  1.00 90.10      S
HETATM 6081  OH2 TIP   161     -19.600  23.788  55.119  1.00 63.82      S
HETATM 6082  OH2 TIP   162      12.071  48.060  40.615  1.00 68.92      S
HETATM 6083  OH2 TIP   163      28.289  31.551  33.446  1.00 58.67      S
HETATM 6084  OH2 TIP   164     -18.857  40.608  48.467  1.00 70.70      S
HETATM 6085  OH2 TIP   165      -2.972   6.632  69.087  1.00 71.62      S
HETATM 6086  OH2 TIP   166       5.019  21.239  11.590  1.00 74.98      S
HETATM 6087  OH2 TIP   167      -4.242 -12.300  64.349  1.00 74.41      S
HETATM 6088  OH2 TIP   168       6.092   5.418  11.062  1.00 58.26      S
HETATM 6089  OH2 TIP   169      -9.930 -16.166  70.042  1.00 77.12      S
HETATM 6090  OH2 TIP   170      27.665  32.448  46.853  1.00 86.11      S
HETATM 6091  OH2 TIP   171     -26.013  31.633  34.322  1.00 63.66      S
HETATM 6092  OH2 TIP   172       8.244   2.428  72.981  1.00 72.20      S
HETATM 6093  OH2 TIP   173     -19.875  32.340  20.985  1.00 65.25      S
HETATM 6094  OH2 TIP   174      11.462  -2.190   5.568  1.00 75.60      S
HETATM 6095  OH2 TIP   175     -24.510   4.225  34.154  1.00 65.70      S
HETATM 6096  OH2 TIP   176       9.210  19.021  23.310  1.00 53.96      S
HETATM 6097  OH2 TIP   177     -18.628  25.940  53.835  1.00 55.14      S
HETATM 6098  OH2 TIP   178       1.594  35.321  17.143  1.00 66.35      S
HETATM 6099  OH2 TIP   179     -35.932  32.773  43.500  1.00 65.83      S
HETATM 6100  OH2 TIP   180       6.610   0.656  77.404  1.00 68.12      S
HETATM 6101  OH2 TIP   181      38.280   4.139  33.513  1.00 76.88      S
HETATM 6102  OH2 TIP   182      23.197  32.109  31.628  1.00 65.86      S
HETATM 6103  OH2 TIP   183       0.495  11.928  51.178  1.00 76.94      S
HETATM 6104  OH2 TIP   184      -9.293  15.487  45.977  1.00 77.80      S
HETATM 6105  OH2 TIP   185      -5.859  38.883  39.260  1.00 53.48      S
HETATM 6106  OH2 TIP   186     -33.933  18.831  40.589  1.00 72.18      S
HETATM 6107  OH2 TIP   187       5.875  12.627  58.910  1.00 79.98      S
HETATM 6108  OH2 TIP   188       2.542  10.779  55.129  1.00 69.62      S
HETATM 6109  OH2 TIP   189       6.354  22.715  29.312  1.00 83.68      S
HETATM 6110  OH2 TIP   190      10.534  12.785  55.689  1.00 68.13      S
HETATM 6111  OH2 TIP   191     -19.033   3.122  60.501  1.00 71.79      S
HETATM 6112  OH2 TIP   192      15.573   5.668  55.157  1.00 82.05      S
END
```

FIGURE 25 CON'T